S. HRG. 103-593

COMPETITIVENESS OF THE U.S. BIOTECHNOLOGY INDUSTRY

HEARING

BEFORE THE

SUBCOMMITTEE ON SCIENCE, TECHNOLOGY, AND SPACE

OF THE

COMMITTEE ON COMMERCE, SCIENCE, AND TRANSPORTATION UNITED STATES SENATE

ONE HUNDRED THIRD CONGRESS

SECOND SESSION

MARCH 23, 1994

Printed for the use of the Committee on Commerce, Science, and Transportation

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COMPETITIVENESS OF THE U.S. BIOTECHNOLOGY INDUSTRY

WEDNESDAY, MARCH 23, 1994

U.S. SENATE,
SUBCOMMITTEE ON SCIENCE, TECHNOLOGY,
AND SPACE OF THE COMMITTEE ON COMMERCE,
SCIENCE, AND TRANSPORTATION,
Washington, DC.

The subcommittee met, pursuant to notice, at 2:45 p.m., in room SR–253 of the Russell Senate Office Building, Hon. John D. Rockefeller IV (chairman of the subcommittee) presiding.

Staff members assigned to this hearing: Elizabeth Inadomi, staff counsel, and Patrick H. Windham, senior professional staff member; and Louis C. Whitsett, minority professional staff member.

OPENING STATEMENT OF SENATOR ROCKEFELLER

Senator ROCKEFELLER. I am very much looking forward to this hearing, I might say, today, not only because we have a very good set of panels, but we have an extraordinarily interesting subject. And I am very happy about it, and I want you to know that up front. This begins, in a sense, our subcommittee's look at the biotechnology industry and its role in the American economy. And we intend to be rather precise and thorough about this.

In the past, the subcommittee has examined Federal funding of biotechnology research, such as the Human Genome Project. And today, we want to look at the big picture.

Rather than focus on specific technologies, we want to learn more generally about an important industry created in large part by many years of Federal investment in this particular category of technology so that we can think about next steps.

Last week, the Senate completed, after more time than it should have taken, a debate on Senate bill 4, which was the National Competitiveness Act of 1994. And I believe the biotechnology industry and its workers had a stake in the outcome of that debate. Those of us supporting the bill did so and are doing so to try to advance the relationship between Federal investment in science and technology and the economic strength and competitiveness of U.S. firms. We do not think that when the U.S. Government and industry, on a prudent basis and where appropriate, work together is a bad idea. We think it is a good idea. And particularly if industry has the lead.

My colleague, Senator Burns, who I want to state has another hearing at the time and will get over here when he can. So, I need

to apologize to all folks from within 200 miles of Bozeman. He will be here, but he is at another hearing that he has to do right now.

Anyway, Senator Burns and I know that with the right environment, a direct link can be forged between Federal investment into research and technology development and the economic health of our Nation. That is something that we care about, and the President has made it a part of what runs through all of his policies.

The growth of the U.S. biotechnology industry over the past 20 years, which corresponds with the investments made by the National Institutes of Health and a lot of other Federal agencies, illustrates this relationship. So, the U.S. biotechnology industry presents the new American dream. The scientific discovery of DNA and the subsequent ability to manipulate genetic material has created new markets, new jobs and new imagination for the American people.

Public investment in biotechnology has laid the groundwork for a diverse industry of small businesses to grow and flourish. New drugs have been designed using biological tools which are more effective in treating disease. New microorganisms have been developed to break down specific toxic waste in hazardous sites. Federal funding invested in biotechnologies over the years has helped to train many of the world-class cadre of scientists and engineers who have launched and now work in the 1,200 small biotechnology firms across this country.

So, here we see the interaction between Government, industry, and academia as a dynamic and as an important component in the success of this very high-technology industry.

The subcommittee's job is to watch over and authorize the Federal programs and funds for research and development administered by the National Science Foundation, the National Institutes of Standards and Technology, and NASA, in addition to other agencies. The homegrown biotechnology industry holds the promise of expanding our frontiers of knowledge, improving the quality of life, and strengthening our economy.

To me, this is a mixture of benefits that we hope to see from supporting research in technology.

So, today, I hope we are going to get a better understanding of this industry's potential contributions to more economic growth and job creation, as well as whatever may be on the minds of those who are on the panels. The industry is still relatively very young. It is not yet the rags-to-riches story in terms of profits. Obviously, the success or failure of the biotechnology industry rests on a combination of an array of Government policies and private decisions.

The Federal Government's investment in this part of science and technology is just one piece of the puzzle. Again, I want to put that into perspective.

So, we are ready to begin. I encourage the witnesses to look at the big picture with us—even to peer into crystal balls out into the future as far as you can see. That will assist the subcommittee to promote public policies and investments that will reap the economic and social benefits through this very important industry.

So, we have very good experts with us from the administration, from the biotechnology industry across the country, including Massachusetts, California, Louisiana, and Montana.

The subcommittee will first hear from Dr. Greenwood on the overall U.S. biotechnology industry. You are the Associate Director for Science in the Office of Science and Technology Policy; and Ms. Conte, president of a biopharmaceutical firm and representative of the biotechnology industry organization.

The second panel will be comprised of representatives from three specific market segments of the biotechnology industry. Dr. Jacobsen, dean of the College of Agriculture at Montana State University; Mr. Perez of Environmental Remediation, Inc.; and Mr. Skaletsky of GelTex, will testify.

And since I have nobody to turn to for opening comments, Dr. Greenwood, you are on.

[The prepared statement of Senator Hollings follows:]

PREPARED STATEMENT OF SENATOR HOLLINGS

The Subcommittee on Science, Technology, and Space is holding a significant hearing today on the competitiveness of the U.S. biotechnology industry. Federal investment in science and technology not only increases our knowledge but creates opportunities for new markets and economic growth in the United States. The U.S. biotechnology industry, which has created an opportunity for 23 new drugs to be on the market and close to 300 drugs awaiting approval, and with new opportunities for biotechnology applications in agriculture and environmental clean-up, should contribute to our Nation's global competitiveness.

The development of the biotechnology industry is similar to another high technology industry, the American electronics industry. Small electronics firms evolved in the 1960's as the Department of Defense funded universities and companies to develop computers. With biotechnology, especially biopharmaceuticals, the National Institutes of Health (NIH) funded universities and worked with companies to explore tools which could manipulate genetic material. Like electronics, the utility of biotechnology applications spans a variety of industries. Biotechnology advancements have improved crops to resist diseases, pests, drought, and frost and have created new drugs designed to target disease for humans and animals.

The federally created market for clean-up of hazardous sites has generated interest in biotechnology applications to environmental remediation. For the past few years, Congress has appropriated about $5 billion per year to clean up Federal sites which have generated hazardous wastes over years of operation. Naturally occurring and genetically engineered microorganisms can help to restore soil and water contaminated by toxic organic wastes.

The burgeoning biotechnology industry faces certain financial hurdles, particularly given the enormous requirements for small U.S. biotechnology firms to raise capital, especially in later stages of product development.

Better understanding of the interaction between the biotechnology industry and public policy is needed if we are to continue to invest in high technologies for long-term economic growth and competitiveness of U.S. firms. This hearing give us more information about these issues, and I look forward to the testimony of our witnesses.

STATEMENT OF M.R.C. GREENWOOD, Ph.D., ASSOCIATE DIRECTOR FOR SCIENCE, OFFICE OF SCIENCE AND TECHNOLOGY POLICY, THE WHITE HOUSE

Dr. GREENWOOD. Thank you very much. I am delighted to be here, Mr. Chairman, especially after just a few months in Washington, and having had the pleasure of being before this subcommittee just in November—which seems, at this point, some time ago. But I am delighted to have another opportunity to speak with you.

I think this is a very important time and timely hearing that you are having, especially, as you have just noted, with the passage of S. 4, which lays out the broad strokes of how the administration's policies should develop and how we should be looking forward to enhancing the national competitiveness of our country's industries.

This is also, I think, a particularly important time for the biotechnology industry and for biotechnology policy for the biotechnology industries. I would prefer to use the term "biotechnology industries," because I think, as the witnesses will illustrate and as I firmly believe myself, this is a group of industries sharing some very common technology, but addressing a lot of different issues which are related to emerging national goals, particularly those related to health, environmental safety and, in some cases, personal fulfillment.

I am a relative newcomer to Washington, as you know. And prior to my appointment here at OSTP as the Associate Director for Science, I was the dean of graduate studies at the Davis Campus of the University of California. And Davis had the good fortune to have served as a magnet, attracting a growing number of biotechnology companies of a variety of sorts in recent years. The majority of those in the Davis area are focusing their interests on agricultural biotechnology.

In addition, my own research into the genetic predisposition of obesity employed molecular techniques that are the foundation of today's biotechnology industries. So, I have both firsthand knowledge and a deep personal interest and personal excitement that the promise of biotechnology has for us as we try to attack such global problems as environmental pollution, hunger, depletion of energy reserves, and human and animal disease.

The Clinton administration is very much in support of biotechnology. We hope to be perceived that way, and I think that the administration has already done a number of things that are important. Biotechnology, as you know, is a result of decades-long private and public investment in fundamental research, including, for example, the seminal research on the growth factors that came out of the 1970's war on cancer.

And as you have noted yourself, much of the basic information on which this industry is founded and which gives it its pioneering spirit in many ways as it leads us into the 21st century and opens a lot of new opportunities for us in the global market and global competitiveness came from the fundamental research that was supported by the Government in agencies such as NIH, NSF, USDA, and a variety of others as well.

I believe that biotechnology has now matured, to be increasingly more relevant and more than highly promising in an extraordinarily diverse range of applications. The field continues to move very rapidly, requiring not only large capital investments, but also continued vigorous R&D support. As an industry, it is an industry that has the greatest investment in R&D of any of our national industries.

And because of that, because of its newness, because of the tremendous investment in R&D that is necessary to bring it to truly competitive status, the administration is sensitive to these unique challenges facing biotechnology, and is cognizant of the need to allow biotechnology to fulfill its promise safely and rapidly.

These are a few examples of what we are doing to promote progress in biotechnology, although this is not an exclusive list. First, I would list the support of fundamental science as one of the most important things that the administration can do to enlist the

support. For fiscal year 1995, the President has proposed the National Institutes of Health budget increase by about 4.7 percent, and we see about a 6-percent increase in NSF over the previous year.

In a time of tight budget caps and very tough budget choices, and in an increasingly constrained discretionary component of the budget, which I certainly do not need to reiterate to you, I think this is indeed evidence of the importance that the administration places on fundamental discovery, particularly in areas of biotechnology.

Senator ROCKEFELLER. It is almost clinical to trace what goes up in the Clinton budget and what goes down. What goes up usually is what you are working on. It is amazing.

Dr. GREENWOOD. That is right. And it certainly shows fidelity to the overall administration policy of investing in our future and investing in people and ideas.

Another thing I would say that is important to the biotechnology industry is the establishment of the National Science and Technology Council, which, as you know, was established on November 23 by an Executive order signed by the President. The NSTC Council has a number of committees, one of which is called the Fundamental Science Committee, which is chaired by Harold Varmus, Neal Lane, and myself, under which the Biotechnology Research Subcommittee is now a main subcommittee of the Fundamental Science Committee.

Although for 1995 the administration is not conducting a comprehensive budget analysis of biotechnology research as was performed in the previous two years, the Biotechnology Research Subcommittee is concentrating its efforts on the conduct of an ongoing indepth analysis of Federal programs, and identifying areas of particular promise and opportunity for scientific and technological progress in biotechnology.

Senator ROCKEFELLER. Does that mean trying to measure their competitiveness?

Dr. GREENWOOD. There is an effort, certainly, to measure their competitiveness, and also to talk about the areas of biotechnology which have previously not been the dominant areas of biotechnology as we have supported them in the Government programs.

So, we believe that although the analysis of the data collected from the past 2 years from the research programs in the budget inventory, if you will, has been extremely helpful in helping us to know what we have done and how that money is distributed, and it was useful in a time of growing budgets in helping us to gain priority for some additional funding for the biotechnology effort, this is probably the time to analyze the gaps in program and the importance of the programs and the ways in which we can strengthen the programs we have, as well as looking forward to future investments.

As you know, the health-related biotechnology research has represented, by far, the major component of the Federal investment. And this, we hope, we will continue to be a high national priority.

However, the pattern of research support, as I said just a moment ago, has left some important gaps in our knowledge, underly-

ing future applications in critical areas which are now important to our articulated national goals beyond health—such as biotechnology related to environmental remediation and prevention of pollution, biotechnology as it relates to manufacturing and bioprocessing, biotechnology as it relates to agricultural research, and also research on the social impact of biotechnology, and also examining the infrastructure and training needs that biotechnology and the biotechnology industries will need in future years.

In addition to the administration's biotechnology research support activities, an area I should probably mention, is the cooperative research and development agreements, or CRADA's, which is another mechanism by which the administration is fostering the growth of technology. As you know, these represent tremendous health care and economic opportunities for the country.

Unfortunately, over the past year, we have heard that several companies have indicated that they would no longer pursue the establishment of CRADA's with the NIH as a result of an agency requirement that participating companies agree prospectively that any products resulting from such agreements be reasonably priced.

Senator ROCKEFELLER. Dr. Greenwood, why is that? How do you analyze that, the drop in the CRADA's, and what do we do? I am sorry to interrupt, but this is so important.

Dr. GREENWOOD. That is perfectly fine, Senator.

I do not know that we have a perfectly adequate analysis, but it is the case that with the institution of this reasonably priced clause in the NIH CRADA's, which is not found in CRADA's associated with other agencies, we have heard complaints, particularly from the pharmaceutical industry, that this decreases the incentives for them to cooperate with the Government and to invest in these CRADA's.

I think that we probably need some additional ongoing analysis of this. I understand that the NIH is indeed looking into this in some detail. It was reported in the Journal of NIH Research that there was a committee established to look into this and see how they could improve their relationship with the CRADA's.

Senator ROCKEFELLER. So, the reasonable price clause is what you think is—because it somehow potentially hints at some constraint of some sort?

Dr. GREENWOOD. That is right. This is my understanding. I think that the industry representatives will be able to tell you in enormous detail exactly what their perception of this reasonable price clause restriction in the NIH CRADA's means to them. I would not want to say that I am personally convinced that that is the only reason that the CRADA's are a problem. So, I would not want to be misunderstood on that.

Senator ROCKEFELLER. OK. Thank you.

Dr. GREENWOOD. Another issue that is of considerable interest, of course, is the intellectual property protection. It is the development of biotechnology and the tools which support it that have raised several contemporary issues that affect the commercialization and vitality of the biotechnology industries. Only a few years ago, the entire international biomedical research community received a crash course in intellectual property protection when NIH applied for patents on a large number of DNA fragments.

And although NIH has declined to appeal a negative decision from the Patent and Trademark Office on these applications, it has become evident that this technology, and perhaps others, may be moving ahead at a pace that outstrips the evolution of case law. And this, once again, speaks to the sort of pioneering, cutting-edge side of the biotechnology industry. It is challenging us in many ways to think about our policies for the future and for its competitiveness.

Another point I would like to touch on is the need for a thoughtful, sensitive, and, above all, clear regulatory framework that encourages innovation and enables us to meet our national social goals objectively and efficiently.

As part of the technology initiative, the President and the Vice President stated "To improve the environment for private sector investment and create jobs, we will ensure that the Federal regulatory policy encourages investment in innovation and technology development that achieves the purposes of the regulation at the lowest possible cost," and as you know, we are working very hard to harmonize regulatory policies and risk-based assessment across agencies.

Finally, I would say that within OSTP and within the other executive offices we are working on a new coalition, attempting to build a new coalition in which OSTP is playing a very significant role with the Council of Economic Advisors, the National Economic Council, and the Health Security Act folks and the Domestic Policy Council, along with the Office of the Vice President, to begin to define the new horizons for the 21st century for biotechnology and to establish mechanisms for working with industry to move forward with this industry and with its concerns for competitiveness and the programs and policies that would facilitate tremendous competitiveness for the future as we look forward to the next year or so of working together.

Thank you.

[The prepared statement of Dr. Greenwood follows:]

PREPARED STATEMENT OF DR. M.R.C. GREENWOOD

Thank you Mr. Chairman and members of the Subcommittee. I am pleased to appear before you to address an issue of great importance to me, to Dr. Gibbons, to the Clinton Administration, and, I firmly believe, to the Nation. That is—the competitiveness of our domestic biotechnology industry. Or, as I would prefer to say, the biotechnology industries. The reason that I make this point is that biotechnology is not a discrete industrial sector but, rather, a set of tools and techniques that have wide application across several industries that I will mention later in my testimony.

I am a newcomer to Washington, having had the honor to appear before this Subcommittee for my confirmation hearing just last November. Prior to my appointment as OSTP Associate Director for Science, I was the Dean of Graduate Studies at the Davis campus of the University of California. Davis has had the good fortune to have served as a magnet, attracting a growing number of biotechnology companies in recent years, the majority focusing their efforts in the area of agricultural biotechnology. In addition, my own research into the genetic predisposition to obesity employed the molecular techniques that are the foundation of today's biotechnology industries.

DNA—deoxyribonucleic acid—is called the universal code because it is present in all living organisms. The methods used for cutting and splicing human DNA and mapping genes to their respective chromosomes, are virtually identical to those used in analyzing all genomes, from monkeys to mice to mosquitoes to tomatoes. Thus, I have had the opportunity to observe and to appreciate biotechnology first-hand. I hope that today I can convey to you some of my personal excitement about the promise of biotechnology—about its power to help us attack such global problems

as environmental pollution, world hunger, depletion of energy reserves and human and animal disease.

When I first arrived at OSTP, I learned that Dr. Gibbons and I share a commitment to the continued vitality of our U.S. biotechnology efforts. More recently, I became aware that during Dr. Gibbons' 14-year tenure as director of the Congressional Office of Technology Assessment, the OTA was cited as having done more for biotechnology than any other government agency. Indeed, the definition of biotechnology put forward in the 1984 report entitled, "Commercial Biotechnology: An International Analysis," is still the standard, a remarkable feat when you consider the dramatic advances that have taken place in the past decade. Another interesting historical note is that the OTA report was released in a hearing convened by then-Representative Al Gore.

I am especially pleased that you are holding a hearing that focuses on the competitiveness of the U.S. biotechnology companies. Despite the fact that the U.S. is generally regarded as the world leader in biotechnology, no one is, or should be, complacent about our situation. There are signs that indicate that biotechnology is at a particularly critical juncture right now, and the future vitality of our domestic capability may rest on what we in the Administration and you in Congress, and our partners in industry and academia, can accomplish together in the coming several years. I look forward to the statements of the other witnesses to gain their perspective on the state of biotechnology in this country.

ROLE OF THE CLINTON ADMINISTRATION IN SUPPORT OF BIOTECHNOLOGY

Biotechnology is special in several ways:

- It is the result of a decades-long public/private investment in fundamental research including, for example, seminal research on growth factors that came out of the 1970s "war on cancer."
- Biotechnology has now matured to be relevant and highly promising in an extraordinarily diverse range of applications of goods and services—especially in the areas of health (diagnostics and treatment), food and fiber production, environmental remediation and restoration, biomanufacturing of fine chemicals and novel materials, and development of renewable alternative energy sources.
- The field continues to move very rapidly, requiring not only large capital investment, but also continued vigorous R&D support. New opportunities are emerging with high frequency—moving in areas of exceptional social rate of return.

It is for these reasons that the Clinton Administration has recognized the vitally important role of biotechnology in stimulating and sustaining the long-term economic growth that creates high quality jobs and protects our environment. Clearly, biotechnology is vital to our success in these endeavors. Many of the initiatives and activities that will promote national economic growth and improved quality of life through technological progress apply equally to the semiconductor and automotive industries, to advanced materials and manufacturing, as well as to biotechnology. The President and Vice President have developed a strategy outlined in the February 1993 document "Technology for America's Economic Growth: A New Direction to Build Economic Strength," and followed by the President's Progress Report published in November. The Administration's science and technology goals include:

- Reaffirming our commitment to fundamental science, the foundation upon which all technological progress is built; and
- Improving the contribution of federally sponsored science and technology innovation to economic growth, job creation and environmental quality by forming closer working partnerships among industry, federal and state governments, workers and universities.

The Administration intends to work directly with entrepreneurs and industries that are improving existing or developing new technologies. These efforts will benefit biotechnology along with other emerging high technology-driven sectors and this effect is both desirable and appropriate. However, it is also apparent that biotechnology seems to be approaching, or has already reached the limits of our existing systems for technology management and oversight—stressing our regulatory system, our intellectual property protection system and is, perhaps, subject to enhanced sensitivity on Wall Street to real or perceived threats to product development and approval. I am a firm believer in letting market forces determine which products go forward in development. But it is our responsibility to ensure that the government doesn't impose artificial or unnecessary barriers that prevent these forces from taking effect.

The current Administration is sensitive to the unique challenges facing biotechnology and is cognizant of the need to proceed carefully in order to allow bio-

technology to fulfill its promise, safely and rapidly. These are a few examples of what we are doing to promote progress in biotechnology:

SUPPORT FOR FUNDAMENTAL SCIENCE

The ability to enlist the cooperation of the forces of Nature and put them to work in solving many of the problems we face today such as feeding and providing energy to a growing population, improving human health, undoing some of the damage man has wrought on the global ecosystem, and sustaining our natural resources was developed directly as a result of government-funded basic research. I am confident in asserting that biotechnology company CEOs would put government support for fundamental science high on their wish lists.

The Clinton Administration recognizes the enormous rate of return on our public investment in fundamental science. Even in the rather bleak atmosphere imposed by very tight budget constraints, the science agencies have fared relatively well in the President's FY 1995 budget request. For example, the President has proposed that the National Institutes of Health (NIH) budget increase by 4.7 percent, or $517 million over FY 1994. In FY 1994, NIH provided over three-quarters of the $4.3 billion in Federal support for biotechnology research. This increase is especially significant to today's discussion because, historically, NIH has funded the fundamental biology research that is the foundation upon which our biotechnology industries rest. Thus, it is not surprising that the first applications of biotechnology were in the health arena. However, more recently the tools and methods for manipulating the building blocks of life have since diffused throughout other areas of application and are now funded by twelve Federal agencies. Let me take just a moment to describe the process we have put in place to define priorities and to coordinate research support across the Executive Branch agencies.

NSTC AND THE BIOTECHNOLOGY RESEARCH SUBCOMMITTEE

Like other emerging industries, biotechnology is moving toward a phase in which much of the information necessary for advanced product and process development will be proprietary. However, biotechnology-based industry will continue to look to the kind of fundamental scientific research that is supported through the NIH, the National Science Foundation, and other Federal agencies. On November 23, 1993, the President signed an Executive Order establishing the National Science and Technology Council (NSTC), which he will chair. The charge to this new Cabinet-level Council is to establish clear national goals for Federal science and technology investments and to ensure that science and technology policies and programs are developed and implemented to contribute effectively to those national goals.

As one of the first actions taken under this new policy coordination and implementation mechanism, we made certain that the efforts of the Biotechnology Research Subcommittee, which had previously been established under the Federal Coordinating Council for Science, Engineering and Technology (FCCSET), would continue under the new committee structure. The Biotechnology Research Subcommittee is ably chaired by Dr. Laura Powell, Director of the Biotechnology Division of the National Institute of Standards and Technology. This Subcommittee will operate under the aegis of a single, overarching Committee on Fundamental Science which is cochaired by Drs. Lane, Varmus and myself. Biotechnology will also receive attention in at least two other of the nine (9) NSTC committees—e.g. (Health, Safety, & Food; Environment and Natural Resources)

For Fiscal Year 1995, the Administration is not conducting a comprehensive budget analysis of Federal support for biotechnology research as was performed for the two previous years by the Biotechnology Research Subcommittee. Unfortunately, this has been interpreted to mean that we have phased out the activities of the Biotechnology Research Subcommittee. This is not so. Instead, the BRS is concentrating its efforts on extending the scientific and technical foundations necessary to the development of biotechnology, developing the human resources necessary to biotechnology, facilitating the transfer of biotechnology research discoveries to commercial applications and realizing the benefits of biotechnology for human health, agriculture, and the restoration and protection of the environment. These goals are supported through the conduct of an ongoing, in-depth analysis of the programs of the twelve participating Federal agencies and identification of areas of particular promise and opportunity for scientific and technological progress in biotechnology. Analysis of the data collected over the past two years from the research programs and budgets of the twelve member agencies led to two principal conclusions:

- Health-related biotechnology research has represented by far the major component of the Federal investment; this must remain a high National priority.

• This pattern of research support has left important gaps in the knowledge base underlying future applications in critical areas beyond health: in biotechnology related to the environment, to manufacturing and bioprocessing, agriculture, in research on the social impact of biotechnology, and in the infrastructure and training specific to biotechnology research in these areas.

The Biotechnology Research Subcommittee is currently preparing a report on the following areas which promise major contributions:

• *Environmental Biotechnology:* The Federal Government supports research on mechanisms which maintain ecosystem integrity and function; the use of individual organisms, groups of interacting organisms, and their products for environmental rehabilitation; whole ecosystem bioremediation; exploration of organismal diversity from different habitats; development of information concerning the biological properties of different microbes. One popular example of how biotechnology might be put to work in the environment is the use of "oil-eating" or other genetically engineered or naturally occurring bacteria to disperse oil spills or to break down other pollutants into non-toxic by-products.

• *Bioprocessing and Bioconversion:* This portion of the report will describe efficient production of commercially valuable molecules, such as specialty chemicals and biopolymers; the conversion of low-cost raw materials (e.g., biomass or low-grade ores) into useful products; studies of the physiology, biochemistry and genetics of suitable organisms; biosensor development; design and scale-up of bioreactor systems and of separation and purification systems. The accumulation of waste in our landfills is a rapidly growing problem that would be alleviated by the development of biodegradable alternatives to plastics. Innovative products ranging from molded plastic razors to fast food wrappings are being made from corn. Unlike conventional plastics, when composted, the new materials convert into peat-like materials that are suitable for agricultural use.

• *Agricultural Biotechnology:* Key areas of agricultural biotechnology research include: the use of molecular biology techniques for enhancing understanding of basic plant biology, e.g., flower initiation; regulation of gene expression in plants; elucidation of the metabolic pathways leading to production of useful plant chemicals; mechanisms by which plants respond to environmental signals and stress and how plants interact with pests, pathogens and symbionts. Crop plants in the future may be genetically engineered to give gnawing insect pests a fatal case of indigestion. Introduction of the gene coding for an enzyme that is lethal to sap beetles or corn earworms, may offer protection from these pests to figs, peaches, corn, cotton and tomatoes.

• *Marine Biotechnology:* This is a relatively recent focus for U.S. biotechnology research efforts. Of particular interest are: studies to elucidate the molecular genetics, biochemistry and cell biology of marine organisms, their products and processes; applications of molecular biological techniques to an understanding of the role of marine organisms in the global carbon and elemental cycles; studies on molecular adaptations of organisms from extreme environments such as deep sea hydrothermal vents and polar environments; the use of marine viruses in genetic engineering; biodegradation of toxic substances; and studies of nutrition, physiology, reproduction, and genetic makeup of economically important fish and shellfish. Unfortunately, the Chincoteague oyster is under siege from infection with MSX. Rescue through the development of shellfish strains resistant to this microbe would have an immediate impact the local fishing industry and oyster consumers.

SUPPORT FOR BIOTECHNOLOGY RESEARCH THROUGH THE ADVANCED TECHNOLOGY PROGRAM

Biotechnology research and development are supported through several other important mechanisms that I would like to describe. One of those is the Advanced Technology Program (ATP) administered by the Department of Commerce through the National Institute of Standards and Technology (NIST). The ATP is designed to promote the economic growth and competitiveness of U.S. businesses and industry by accelerating the development and commercialization of promising, high-risk technologies with substantial potential for enhancing the Nation's economy. The ATP research priorities are set through an interactive process with industry, by means of competitive proposals from industry and academia aimed at development and commercializing innovative technologies. Out of 400 industry responses to a recent ATP announcement, roughly 10 percent were in the biotechnology area. On January 12, NIST hosted a workshop on biotechnology to explain the procedures necessary to obtain support through the program, and to solicit industry input on setting research priorities that meet the program selection criteria. The workshop

was well attended and indicates strong interest in this program on the part of industry.

One ATP-funded project has resulted in the development of a research tool with enormous potential for screening drugs for treatment of Alzheimer's. A California biotechnology company has developed a transgenic mouse that expresses amyloid, the protein that forms the basis for the development of the neurofibrillary tangles that are characteristic of Alzheimer's. Although it too early to know whether or not the mice will actually develop the disease as it occurs in humans, this is a promising model in which to test compounds for their ability to prevent the changes in brain tissue that underly the disease.

ADDITIONAL ADMINISTRATION BIOTECHNOLOGY SUPPORT ACTIVITIES—CRADAS

Throughout the 1980's, Congress enacted a series of legislation intended to promote the translation of federally-funded research results into useful products. These actions were taken in recognition of the need to offer incentives to both inventors and the private sector to encourage better use of government research. There is abundant evidence that these efforts were successful, having established over 2,000 CRADAs to date, and we are just beginning to see the payoff in terms of commercial development.

This year, instructions have been given to Federal laboratories to devote a growing percentage of their budgets to R&D partnerships with civilian industry. We are emphasizing increased use of cooperative, cost-shared research and development agreements (CRADAs) as well as other cooperative arrangements.

One of the first CRADAs initiated by the National Institutes of Health is noteworthy in several respects. The CRADA between NIH and Genetic Therapy Inc. (GTI) capitalized on technology and expertise in the NIH laboratories of Drs. French Anderson, Michael Blaese and Steven Rosenberg, to launch a new company, a new form of treatment for genetic and other diseases and a new industry sector, that is, gene therapy. Beginning with the first human gene transfer trial initiated in 1988, NIH has now approved 72 clinical gene transfer trials at centers across the nation. Studies involving revolutionary approaches to the treatment of cystic fibrosis, severe combined immune deficiency, advanced melanoma and MDS are now under way or are about to be undertaken. These represent tremendous health care and economic opportunities for this country.

Over the past year, several companies have indicated that they would no longer pursue the establishment of CRADAs with NIH as a result of an agency requirement that participating companies agree prospectively that any products resulting from such agreements be "reasonably priced." While this may seem to be a reasonable request on the part of any consumer, it is considered by some companies to be a significant disincentive to the initiation of cooperative projects between government and industry scientists. This is not an issue that my office has been involved in, but I would hope that all of the relevant views receive careful consideration before any further decisions are made regarding the pricing clause. After all, the public good may be served in many ways, including access to such innovative forms of treatment as gene therapy.

INTELLECTUAL PROPERTY PROTECTION

As drafted by Thomas Jefferson, the U.S. patent system is intended to, "Promote the progress of science and the useful arts, by securing for limited times to authors and inventors the exclusive right to their respective writings and discoveries." This right to exclude others from practicing one's invention has, over time, become a magnet for investors seeking to exploit new technologies and products for commercial purposes. Biotechnology shares this aspect with other emerging high technologies but may be unique in that some of its products, such as enzymes, growth factors or receptors, skirt the edges of what has traditionally been considered patentable. As a result of this added level of uncertainty with respect to intellectual property protection, biotechnology may appear to pose more of an investment risk than other technologies.

Interestingly, it is the development of biotechnology and the tools which support it that has raised several contemporary issues regarding patent law and international trade negotiations. For example, only a few years ago, the entire international biomedical research community received a crash course in intellectual property protection when NIH applied for patents on a large number of DNA fragments. The issue here, for the scientific community, was the wholesale patenting of partial gene sequences for which there was little information on the actual function of the protein products encoded in these sequences. Although NIH recently declined to appeal a negative decision from the Patent and Trademark Office on the first of these

applications, it has become evident that this technology, and perhaps others, may be moving ahead at a pace that outstrips the evolution of case law. As we move into the global marketplace, any problems or uncertainty with respect to protection of intellectual property may become magnified and, therefore, affect the commercialization and vitality of the biotechnology industries.

ENCOURAGING INVESTMENTS IN THE FUTURE WHILE UNDERSTANDING THE CONSTRAINTS OF THE MOMENT

I think it is fair to characterize biotechnology as a set of start-up industries. These are not huge, vertically-integrated companies that support their research and development out of profits from product sales. In fact, most of the biotech firms are still operating in the red and, according to the 1994 Ernst and Young survey, 58 percent have less than 2 years of cash on hand. Add to this picture a very high rate of research spending per employee ($59K per employee, or 81 percent of sales), and you begin to see why biotechnology is heavily dependent on the public and private investment markets to bankroll start-ups and follow-on financing to support product development. This topic is somewhat far afield from my jurisdiction but I am interested to learn from industry. The Administration has taken some steps to improve the long-term, lower cost availability of capital. The President has signed into law tax incentives for private-sector investment in R&D and new business formation, including a targeted reduction in the capital gains tax for investment in small businesses. We will also continue to push on reducing Federal deficits which syphon off savings that otherwise could flow to private capital markets.

MAKING THE RESEARCH AND EXPERIMENTATION (R&E) TAX CREDIT PERMANENT

The 1991 OTA report on Biotechnology in a Global Economy cited the R&E tax credit as a key issue for congressional consideration in protecting U.S. industrial innovation and international competitiveness. In the past, the effectiveness of this credit was seriously undermined because it was extended one year at a time. Under those conditions companies cannot accurately project the real costs of a given R&D project. Research and development, by its nature, requires long-term investment, and businesses will be reluctant to make such commitments without a permanent R&E tax credit. The tax credit was reauthorized for 3 years and we will continue to work toward our goal of making it permanent.

REGULATORY POLICY

The final point I want to touch on is the need for a thoughtful, sensible and, above all, clear regulatory framework that will encourage innovation and enable us to meet our national social objectives efficiently. As part of the Technology Initiative, the President and Vice President stated that,

> "We can promote technology as a catalyst for economic growth by * * * directly supporting the development, commercialization and deployment of new technology; and
>
> "To improve the environment for private sector investment and create jobs, we will ensure that Federal regulatory policy encourages investment in innovation and technology development that achieve the purposes of the regulation at the lowest possible cost."

The Clinton Administration welcomes open discussion and debate as key ingredients to the development of successful regulations. Only through public dialogue can we develop regulations which address the necessary questions in a way that facilitates decision-making by the Government, increases certainty and predictability for industry at the lowest practical cost and that are demonstrably fair to the public interest.

While the regulatory process must be scientifically sound in order to provide the necessary public safeguards, it is also in the public interest to move products into the market as rapidly as possible. New drugs, for example, cannot save lives until they may be safely prescribed. In addition, lengthy approval times are a major disincentive to product development and to investment in the products that face an expensive review. That is why the FDA has instituted a program for the accelerated review of drugs for the treatment of serious and life-threatening conditions. Two very important new drugs illustrate the success of this effort. DNase, a drug for the treatment of cystic fibrosis, the most common inherited disease among Caucasians in this country, was approved 13 months after receipt of the application. Betaseron, which is the first therapeutic agent for the treatment of multiple sclerosis, was recently approved in just one year. However, there are now literally hundreds of new biotechnology products in the development pipeline. FDA must be given adequate funding and staffing to handle the coming avalanche of marketing applications for

these products. Otherwise, there will be long delays before these promising new drugs can reach the people who will benefit from them.

In the agricultural arena, USDA has issued permits for 474 field releases of genetically engineered plants, many more than the total for the rest of the world. These efforts demonstrate how the Clinton Administration is working to create a regulatory climate in which the "clean" industries that are exemplified by biotechnology may flourish.

CONCLUSION

In conclusion, biotechnology offers great promise for the future and has the potential to impact nearly every facet of our lives. The keys to successful innovation and commercialization will be a strong basic research program, fiscal and economic tax policies that encourage investment, a rational regulatory policy and an educated public. This Administration will help sustain the strong research base and fiscal and administrative infrastructure necessary for the continued strength and leadership of our biotechnology-based industries.

The Clinton Administration will work with the research communities in the public and private sectors and the American people to build consensus, so that ten years from now, we can look back and say that the 1990's was the decade of continued vigorous research and also the successful commercialization of biotechnology and biotechnology products in the United States and throughout the world.

I would like to commend you, Mr. Chairman, and the members of your subcommittee, for convening this important hearing and I would be pleased to answer any questions you might have.

Senator ROCKEFELLER. Ms. Conte, why do we not hear from you now, then I can ask both of you questions.

STATEMENT OF LISA CONTE, PRESIDENT AND CHIEF EXECUTIVE OFFICER, SHAMAN PHARMACEUTICALS, INC.

Ms. CONTE. Thank you very much. Again, Mr. Chairman, I appreciate the opportunity to testify here today.

Senator ROCKEFELLER. And I failed to identify your company, and I apologize for that. I only made you a representative.

Ms. CONTE. Do you know the name of my company?

Senator ROCKEFELLER. Shaman.

Ms. CONTE. I will identify it again. I am Lisa Conte, founder, president, and CEO of Shaman Pharmaceuticals, and I am here, of course, on behalf of my own company as well as the Biotechnology Industry Organization, which represents over 500 member companies of the biotechnology industry.

I am a member of an industry that has four distinguishing characteristics. We have very long-term timeframes for the development of our products. It requires a large amount of capital investment. It is very risky, but the results are wonderful new ways of approaching medical answers to unmet medical needs that are out there.

We have been very appreciative of the support of the current administration and support of Members of Congress for this industry, and not only in terms of health care, but also for the impact that it can have on the economy, on the environment, and the continuing leadership role that the United States has taken in innovation in this particular industry.

Senator ROCKEFELLER. Ms. Conte, I hear almost without exception from the pharmaceutical industry, which is not exactly what you are doing, terror about the President's Health Care Act.

Ms. CONTE. Yes, you do.

Senator ROCKEFELLER. Do you want to talk about that? I mean, you do not have to, but if you want to, I would be interested.

Ms. CONTE. I would be happy to talk about that, and I think it is a different type of terror, but a more important type of terror that you hear from the biotechnology industry. The pharmaceutical industry one way or another will still be a pharmaceutical industry, no matter what happens with health care reform. With the biotechnology industry, we may cease to exist in the next 3 to 5 years if some of the current plans in the Clinton health care bill go through.

Senator ROCKEFELLER. Why did you not say that, instead of you were very pleased by what the Clinton administration is doing?

Ms. CONTE. We are very pleased with the support of the biotechnology industry overall, as well as the support from many Members of Congress.

If you want to focus specifically on health care reform, there are some things there——

Senator ROCKEFELLER. Do that, too, and I will not interrupt any more, but I am interested. I am very interested. I mean, I spent some time with the president of Eli Lilly the other day, and it was very helpful to me, and I need to know as much as I can, so tell me everything you can.

Ms. CONTE. OK. I will start with health care reform first, since you brought it up, and that really has to do with our lifeblood—it gets back to the large amounts of capital that we need. Today, Shaman is 5 years old. Today exactly is our fifth year birthday. This company was started 5 years ago on this day with credit cards by myself.

In the past 5 years, I have raised over $90 million for this company. I expect to have my products commercialized in the next 3 to 5 years. I will have to raise at least another $90 million, and that is not going to come from my credit cards. I am very dependent at this time on the capital markets for additional capital to fund my products.

I am in the very unique position that I did two public offerings last year. I did my initial public offering in January, and I did a follow-on offering in November.

I have faced two dramatically different climates. It was a very welcoming climate, great demand for biotechnology issues in January, and we had a very successful offering of over $40 million.

Had I done that offering 2 days later, or planned to do it 2 days later, it would not have happened. I would not have completed my initial public offering and Shaman would not exist today as the stand-alone company it is. I would have had to sell off my technology in order to continue to fund the products.

The reason for that was clearly a combination of some industry-specific events. There were some prominent industry products which did not do well, and the attack of the pharmaceutical industry in the press by the current administration, that decreased our whole industry's value about 40 percent. My stock itself dropped almost 40 percent in 2 days.

Because of that——

Senator ROCKEFELLER. But then did it not go back up over a period of time?

Ms. CONTE. It came back up. It never rose to quite the same level, but it did come back up, but what that did was take a por-

tion—there is a small population of institutional investors that are going to invest in our types of companies. These are companies that are valued over $100 million with no revenues, no profits, and no prospects of those over the next couple of years.

It all of a sudden eliminated a portion of that population who no longer wanted to invest in companies that not only had technology risks, regulatory risk, and financial risk, but now also had the risk that what they are betting on, the products, the profit that they are betting on is going to be regulated by a Government entity that they do not know about.

Senator ROCKEFELLER. And even though the word—the Drug Price Commission is what you are referring to.

Ms. CONTE. The breakthrough Drug Price Commission.

Senator ROCKEFELLER. Even though it does not set any prices, and all it does is comment on, and if the comment—if the price appears to be outrageous to HHS, then they cannot make it part of the reimbursed package, but that combination of things really creates big, big problems, you are telling me.

Ms. CONTE. The perception in the investment community is price controls. What it is, it is debatable. The perception, I guarantee you, with the investment community that I have to go to as a public company is price controls. Because of the uncertainty that I was facing in capital markets and being able to fund my company, I cut back a third of our research. I cut off a whole therapeutic area. My research into diabetes had to stop.

Senator ROCKEFELLER. Did you—and this was right after this came out.

Ms. CONTE. This was in February of last year.

What I did then was kept my eyes open. If there was ever an opportunity last year to be able to raise some more capital, I was going to take it.

That happened toward the end of the year, and I am in very close contact with major investors in this industry, and there is a population of investors who felt that the breakthrough board was not going to happen, that price controls was not going to happen, because it could not happen. It would have such detrimental effects to the long-term development of medical care and the new medical challenges that would arise in the future, it could not happen, and therefore they were going to invest in this industry again.

That, in addition to unsolicited interest from Japanese investors, so those two together allowed me to do a follow-on offering in November. I did have a fair amount of Japanese investors, long-term money. They want to own the company and they want to own it well into the future.

Then that allowed me to open up my diabetes research again, and in the past 5 months it has turned out to be the most prolific discovery program that we have, and we have several interesting compounds that are working in animals, and this is an area where there has been almost no intervention. There is insulin and human insulin, but there are no other treatments, really, in that area.

So, it is very scary to us. It is a survival issue. I am very lucky I have 2½ years' worth of money in the bank. Seven hundred sister biotechnology companies, if they do not raise any more money, will run out of money in the next 2 years, so they have to figure out

some way to get more capital into the company, and so the effects of just the perception right now will affect medical outcomes 10, 15 years down the road because of the long-term nature, again, of the industry, and the risk associated with any individual company.

Senator ROCKEFELLER. We will discuss that further, but I do not want to take you away from what you wanted to say.

Ms. CONTE. Well, that is a good portion of what I wanted to say. [Laughter.]

Some of the other things I wanted to talk about, first I would like to introduce you a little bit to the company, what the vision of this company is, and then talk about some of the situations we are faced with our products, which I think will address the issue of CRADA's, where the industry is coming from.

First of all, Shaman is a biopharmaceutical company that does all drug discovery from plants used traditionally in tropical areas, so what we are doing is leveraging off the knowledge of the medicine man to come up with a more efficient route of drug discovery, and that was the vision of the company 5 years ago, to come up with a more efficient way to discover drugs, as compared with the mass screening, brute force methodologies that are utilized by the major pharmaceutical firms.

In addition, we want to come up with new classes of drugs that are attacking diseases from totally new points of view, and that is one of the great opportunities of working with plant material. Mother Nature is a different, a more unique, and in some senses a better chemist than man can ever be, and what we typically find is totally new classes of breakthrough drugs that do provide new needs to unmet medical needs that are out there.

We also have a nonprofit—that is the birthday that is today. It was established the first day with the company. It is called the Healing Forest Conservancy, and it is through this nonprofit that we return benefits to all the individuals, all the cultures, all the communities, and all the countries that we work with around the world. At this point we work with 35 different countries in tropical areas.

We have been successful for the state that we are on now. In our first 2 years of operations, we moved two products all the way from discovery concept to human clinical trials. That is the fastest timeframe for any startup pharmaceutical.

The first product is in clinical trials right now in AIDS patients, for herpes infections that are resistant to all currently available treatment, so this is getting back to Mother Nature approaching disease from a new point of view.

The second product is in clinical trials for respiratory syncytial virus. That is basically a childhood flu. It is the most important disease around the world in children under the age of 5 in terms of prevalence and severity. It will kill—RSV and complications of the disease will kill approximately 5 million children each year, including several thousand otherwise healthy children in the United States every single year.

Now, a very interesting feature of this product is that through a longstanding CRADA that we had with the NIH in a collaboration, we found that it also had activity against the hantavirus, and the hantavirus is more popularly known as the four corners dis-

ease, the four corners mystery disease that killed several individuals on an Indian reservation last summer and now has killed several dozen Americans and has spread well beyond the four corners.

In order to continue the development of the product for this application, it required a new CRADA, and a new CRADA had the requirement of this new reasonable pricing clause in it. This was about the same time that I was doing my follow-on offering. Investment bankers, investors, said no way could I sign such an agreement that gave the NIH the right to evaluate my pricing on a product that I discovered, that I developed, that I own all the technological rights to.

So, we could not sign the CRADA, we could not collaborate on the research, and now the development of that product has been dramatically hindered. It is going forward, but it has to compete for other internal company resources.

So, I say this, I talked about Shaman, to illustrate those four points that I mentioned. It is a business that is very risky, it requires large amounts of capital, it is very long term, the implications of policies decide on now may not be seen for many years to come, but the effect is wonderful new ways of treating unmet medical needs.

We are looking forward to a continued partnership with the administration. We think this is an ongoing dialog. You can bet there are going to be new challenges in the future that are going to require biological answers. Examples, of course, are AIDS, drug-resistant diseases such as TB, agricultural disasters that have hit, and what we want to retain is the incentives for this industry so that it has the flexibility and the viability to answer those challenges in the future.

[The prepared statement of Ms. Conte follows:]

PREPARED STATEMENT OF LISA CONTE

Good afternoon. My name is Lisa Conte, and I am the president and CEO of Shaman Pharmaceuticals. Shaman Pharmaceuticals is discovering and developing new plant-based pharmaceutical products. Using a novel and cost-efficient discovery process, Shaman's focus is the isolation of active compounds from tropical plants that have a history of medicinal use.

Since it began operations in May, 1990, Shaman has advanced two products from concept to the clinic. The first, Provir, is an oral product that has demonstrated activity against a broad spectrum of respiratory viruses. The second, Viren, is a topical antiviral product for the treatment of herpes simplex virus. Shaman's product pipeline contains approximately 290 already-identified active plant extracts. However, the company is focusing its research efforts on antiviral, antifungal, analgesia and diabetes therapeutic targets, all of which represent large market opportunities due to the limitations of available treatments.

Shaman Pharmaceuticals, as part of its commitment to conserve the rain forest while developing novel pharmaceuticals from tropical plant sources, formed an independent nonprofit group, The Healing Forest Conservancy (HFC) in 1989. The HFC is committed to conserving biocultural and biological diversity and to sustaining the development and management of the natural and biocultural resources that are part of the heritage of native populations. Working directly with local peoples and local organizations, it is helping native people participate in and share responsibility for the process of plant collection as well as supporting worldwide conservation efforts. A portion of the profits Shaman generates will be donated to this non-profit entity.

I am testifying here today on behalf of the Biotechnology Industry Organization (BIO), the international trade organization to serve and represent the emerging biotechnology industry in the United States and around the globe. As the leading voice for the biotechnology industry, BIO represents over 500 companies of all sizes engaged in the development of products and services in the areas of agriculture, biomedicine, diagnostics, food, energy and environmental applications.

The biotechnology industry appreciates the interest of this subcommittee in the biotechnology industry. We look forward to working with this subcommittee on many policy issues of interest to high technology entrepreneurs.

DEFINITION AND APPLICATIONS OF BIOTECHNOLOGY

Let me start by attempt to define our industry and the technology we create. Biotechnology is the application of engineering and technological principles to living organisms or their components to produce new inventions or processes. An important branch of biotechnology is genetic engineering, or recombinant DNA technology, which concerns the analysis and alteration of genes and proteins. These sciences are of vital importance to worldwide progress in medicine, agriculture and the environment.

A large portion of the biotechnology industry is focusing on the development of medical products. To date, twenty-three genetically engineered drugs and vaccines are now commercially available to prevent or treat such diseases as AIDS, diabetes, dwarfism, hepatitis, heart attacks, anemia, leukemia, renal cancer, organ transplant rejection, and Kaposi's sarcoma. The techniques discovered by the biotechnology industry are also used to assist in the discovery of drugs from traditional sources and unique applications. Drugs and vaccines that are being developed by emerging biotechnology and pharmaceutical companies will treat such intractable diseases as cancer, arthritis, Alzheimer's, and genetic disorders.

Hundreds of biotechnology products are being marketed for the diagnosis of such medical conditions as pregnancy, cancer, hypercholesterolemia, and AIDS. Many more diagnostic products are being developed by emerging biotechnology companies.

Another major area of focus for biotechnology companies is new agricultural products. Agricultural biotechnology promises to improve the nutrition, taste, and yield of our food crops while lowering farm input costs and offering environmental benefits over existing agricultural technologies through the net reduction of chemical pesticide use. For example, several biopesticides are now available to prevent crop losses due to insects by using organically produced, nontoxic, biodegradable proteins rather than synthetic chemicals. One that was approved in 1993 is Crop Genetics' Spod-X bioinsecticide, a proteinencapsulated virus used to protect vegetables and flowers against beet worms.

In addition to benefiting American consumers, farmers, and the environment, advances in agricultural biotechnology (such as development of drought and disease-resistant crops) offers perhaps the only hope for agricultural self-sufficiency and economic stability in developing countries. Agricultural biotechnology's products are expected to be the largest contributors to improved food yields over the next 20 years.[1]

There are also the chemical and environmental sectors of the biotech industry which are researching products to improve chemical and fuel production and clean up environmental pollutants. This sector is in the early development stage: Bioremediation, the use of microorganisms to degrade toxic materials to harmless substances, is proving to be a cost-effective alternative to land fills and incineration for both pollution prevention and remediation. In addition, these sectors are exploring new research areas, including biosensors, which combine biotechnology with materials and electronics technology to produce monitoring devices with potential applications in health care, pollution control and control of industrial processes. These devices could be used, for example, to monitor glucose or cholesterol levels or to detect water and air pollutants.

BIOTECHNOLOGY INDUSTRY OVERVIEW

The biotechnology industry consists of approximately 1,300 companies, of which 235 are publicly traded. Approximately 525 of these are biotherapeutic companies, while 344 are diagnostic biotech companies, 191 are ag-biotechnology companies, and approximately 100 firms represent the chemical and environmental segments of the industry. Ninety-nine percent of the companies in this industry have 500 or fewer employees and less than 1 percent are profitable. The industry currently employs over 100,000 people in high-skill, high-wage jobs, a 23 percent increase over 1992. The biotech industry had revenues last year of $10 billion, a 20 percent increase over 1992. Finally, there was a net loss of $3.6 billion in 1993, an increase in losses of 6 percent over 1992. The biotechnology industry, in fact, has never had a profitable year.

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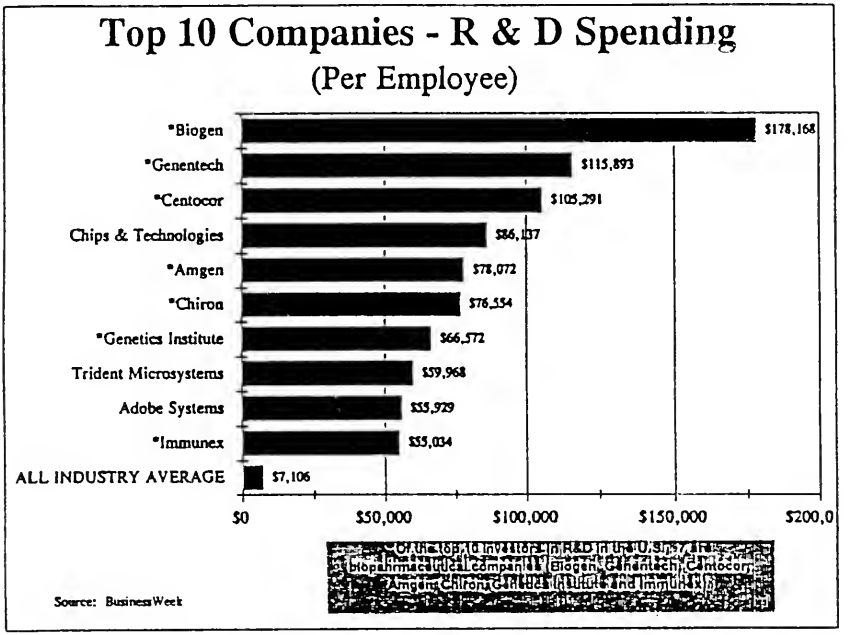
[1] Ernst & Young, Biotech 94 Long Term Value Short Term Hurdles, Eighth Annual Report on the Biotech Industry, 45 (1993).

One reason that the industry has consistently shown a net loss is that it is not yet fully commercialized and companies lack product revenues. Another reason is the amount of capital the industry puts into research and development.



The biotechnology industry is the most research intensive industry in the history of civilian manufacturing, based on R&D as a percentage of revenues and on a per employee basis. In a 1993 survey by Business Week[2] seven of the top ten firms in the U.S. in terms of research expenditures per employee were biotechnology companies—Biogen ($178,168 per employee), Genentech ($115,893), Centocor ($105,291), Amgen ($78,072), Chiron ($76,554), Genetics Institute ($66,572), and Immunex ($55,034). On average biotech firms spend $59,000 per employee on research. The U.S. corporate average was $7,106. Ernst & Young reports that biotechnology companies spent $5.7 billion on research in 1993, a 14 percent increase over 1992.[3]

COMPETITIVENESS OF BIOTECHNOLOGY INDUSTRY

The United States currently has the dominant biotechnology industry when compared with any other country in the world. The former White House Council on Competitiveness stated that, "American researchers developed much of the basic science of the new biotechnology, and the United States continues to lead the world in the commercialization of most emerging biotechnology products."[4] Precisely because the U.S. is preeminent in the field of biotechnology, it has become a target of other country's industrial policies.

In 1991, the Office of Technology Assessment (OTA) found that Australia, Brazil, Denmark, France, South Korea and Taiwan (Republic of China) all had targeted biotechnology as an enabling technology. Furthermore, in 1984, the OTA identified Japan as the major potential competitor to the United States in biotechnology commercialization.[5] The former White House Council on Competitiveness agreed, observing that "foreign governments have targeted biotechnology as of vital economic importance," with Japan in particular mounting a challenge to continued U.S. pre-

[2] Peter Coy et al, "In the Labs, the Fight to Spend Less, Get More," Business Week, (June 28,1993), 102-127.

[3] Ernst & Young, Biotech 94 Long Term Value Short Term Hurdles, Eighth Annual Report on the Biotech Industry, VIII (1993).

[4] The President's Council on Competitiveness, Report on National Biotechnology Policy, 4 (February 1991).

[5] U.S. Congress, Office of Technology Assessment, Biotechnology in a Global Economy, 243 (October 1991).

eminence in biotechnology "in the same way that it earlier targeted the semiconductor and consumer electronic industries." The Council further stated that "European investment in the new biotechnology is close to that of the United States, and Europe actually leads in the production of monoclonal antibodies."[6]

The OTA also identified the manner in which Japan had targeted biotechnology. The report stated,

> "In 1981, the Ministry of International Trade and Industry (MITI) designated biotechnology to be a strategic area of science research, marking the first official pronouncement encouraging the industrial development of biotechnology in Japan. Over the next few years, several ministries undertook programs to fund and support biotechnology."

One of the Japanese ministries, the Ministry of Health and Welfare (MHW), instituted a policy whereby existing drugs would have their prices lowered, while allowing premium prices for innovative or important new drugs, thus forcing companies to be innovative and to seek larger markets.[7]

It is widely recognized that the biotechnology industry can make a substantial contribution to U.S. economic growth and improved quality of life. For example:

- The National Critical Technologies Panel, established in 1989 within the White House Office of Science and Technology Policy by an Act of Congress,[8] calls biotechnology a "national critical technology" that is "essential for the United States to develop to further the long-term national security and economic prosperity of the United States."[9]
- The private sector Council on Competitiveness also calls biotechnology one of several "critical technologies" that will drive U.S. productivity, economic growth, and competitiveness over the next ten years and perhaps over the next century.[10]
- The United States Congress' Office of Technology Assessment calls biotechnology "a strategic industry with great potential for heightening U.S. international economic competitiveness." OTA also observed that "the wide-reaching potential applications of biotechnology lie close to the center of many of the world's major problems—malnutrition, disease, energy availability and cost, and pollution. Biotechnology can change both the way we live and the industrial community of the 21st century." [11]
- The National Academy of Engineering characterizes genetic engineering as one of the ten outstanding engineering achievements in the past quarter century.[12]
- Lester Thurow and Robert Reich have recommended policies that shift investment and resources away from declining segments of manufacturing and into services and emerging industries such as biotechnology and computers.[13]

The importance of the biotechnology industry to America's competitiveness warrants development of a comprehensive biotechnology strategy that takes into account the industry's strengths, weaknesses and needs.

KEY POLICY ISSUES FOR BIOTECHNOLOGY INDUSTRY

Key policy issues that affect the competitiveness of the U.S. biotechnology industry include six thematic issues: basic research and technology transfer, regulatory policy, intellectual property protection, trade policy, the financial environment, and health care reform.

Let me say to begin with that the biotechnology firms are quintessential entrepreneurs. We take risks with our pay by substituting stock options for fixed compensation. We risk our capital by investing in a firm with no revenues or dividends. We risk failure by focusing on cutting edge research. We are willing to risk strict regulatory review of our products before they go to market. Our most fervent wish is for the government to ensure that we have the opportunity to succeed or fail based on the marketplace's determination of the value of our products.

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[6] The President's Council on Competitiveness, Report on National Biotechnology Policy, 5 (February 1991).

[7] U.S. Congress, Office of Technology Assessment, Biotechnology in a Global Economy, 244–245 (October 1991).

[8] National Competitiveness Technology Transfer Act, Pub. L. No. 101-189, 103 Stat. 1352 (42 U.S.C. § 6681 et seq.).

[9] White House Office of Science and Technology Policy, Report of the National Critical Technologies Panel, 7 (1991).

[10] Council on Competitiveness, Gaining New Ground: Technology Priorities for America's Future, 6 (1991).

[11] Congress, Office of Technology Assessment, New Developments in Biotechnology: U.S. Investment in Biotechnology-Special Report, 27 (July 1988).

[12] National Academy of Engineering, Engineering and the Advancement of Human Welfaree: 10 Outstanding Achievements 1964–1989, 2 (1989).

[13] Choate, Pat, The High Flex Society—Shaping America's Economic Future, 169 (1986).

We are also practical about government. We recognize that we benefit from certain government activities and know that we need government's help to protect our legitimate interests.

BASIC FEDERAL GOVERNMENT RESEARCH AND SCIENCE PROGRAMS

The U.S. biotechnology industry is competitive in international markets in part because of the large investment of the Federal government in basic research. Biotechnology companies conducting biomedical research are connected to the National Institutes of Health (NIH) in many ways. Several of the industry's top scientists were trained at NIH or NIH-funded institutions. Many biotechnology companies grew out of university-based research, largely funded by NIH. Many more biotechnology companies license patents from NIH or the universities. Still other biotechnology companies have Cooperative Research and Development Agreements (CRADAs) with various federal laboratories including NIH.

In addition, biotechnology research is being conducted by numerous other federal agencies. The National Institute of Standards and Technology (NIST) is establishing an interdisciplinary program to address the critical areas of biotechnology, including bioprocess engineering to improve the manufacture of pharmaceuticals, bulk and specialty chemicals and alternative fuels. NIST also administers the Advanced Technology Program (ATP), which provides support on a cost-sharing basis to industrial R & D projects with a significant potential for stimulating economic growth and improving the competitiveness of U.S. industry. The National Oceanic and Atmospheric Administration (NOAA) is conducting research which will advance marine biotechnology. Also, the National Science Foundation (NSF) is actively supporting research critical to biotechnology. One example of this is the development of the NSF Biotechnology Research initiative, which was launched in fiscal year 1993 and is being expanded in fiscal year 1994.

The federal government also fosters biotechnology research through Small Business Innovation Research (SBIR) grants. These are awarded through an intra-agency program, whereby various federal agencies are required to dedicate a percentage of their research budget to U.S. firms conducting R & D into innovative technologies. Businesses compete to receive these grants from the agencies that are required to participate. The National Institutes of Health (NIH), for example, has the largest SBIR program because they have the largest research budget of the federal agencies that are involved. Numerous biotech companies have been awarded grants through this program. The industry sees these grants as an opportunity to fund research and development that otherwise might not be performed. BIO supports continued strong funding for all of the federal programs mentioned above.

S.1537 AND NIH CRADAS

We support the goals of S. 1537, the Technology Commercialization Act of 1993, introduced by the Chairman of this Subcommittee Senator Rockefeller and Senator DeConcini and believe it would enhance the competitiveness of the U.S. biotech industry. The bill would ensure that the ownership of any invention or other intellectual property developed by a CRADA belongs to the company or companies which develop it. We appreciate that the bill focuses on the vital role which private businesses play in commercializing government funded basic research. The Chairman's statement of October 7, 1993, showed a sophisticated understanding of the technology commercialization process when he said:

- "* * * the development of new technology cannot, by itself, bring any * * * gains in our national income, our social well-being, and our international competitiveness. The critical factor in producing these benefits is the commercialization of technology."
- "Only when technology is commercialized can it create jobs, production and profits."
- "[I]t is today's earnings from commercialized technology which will enable our manufacturers to undertake the research and the investments that lead to the next generation of technology and commercialization and to more jobs for Americans tomorrow."
- "It is obvious * * * that commercialization of technology and industrial innovation in the United States is more likely to occur when the private sector, rather than the Government, has title to the intellectual property."

We especially appreciate the emphasis in the legislation on the Government laboratory receiving "reasonable compensation" for the technology that is transferred. Our companies are willing to negotiate royalties or other arrangements with the Government when they license and then commercialize intellectual property transferred by the Government.

The biotechnology industry has two concerns about the current technology transfer process of the agency which conducts most of the basic biomedical research, the National Institutes of Health. The transfer of technology by NIH often involves a license of a patented invention and the agreement by the licensee to pay royalties to the patent holder for products derived from the patent. These royalties provide a return to the government if and when the research leads to product sales for a private company. A similar license-royalty system is used extensively in relationships between private companies for the same purpose.

Unfortunately, starting during the last Administration, NIH insists on inserting a clause into it's CRADA's which impose a reasonable price clause. As the Office of the Inspector General of HHS has recognized in a recent report, this system has deterred technology transfer. A recent article in Science cites NIH officials attributing the price control clause for the decline in CRADAs.[14] NIH is unique among the Federal agencies which sponsor CRADAs in requiring the review of the prices of the medicines which are based on its patents. This government review of price process applies now only to licenses issued by NIH.

Our companies are willing to negotiate royalties or other agreement with NIH. The parties can determine when the patent is licensed the forms and conditions of an agreement, including whether royalty payments are appropriate and if so how much. But, they are not able to plan if the NIH reserves the right to set the price for the medicine if and when it is sold to the public.

This use of an arbitrary "reasonable price clause" is undermining the transfer of NIH patents to private companies and the competitiveness of our industry. Many private biomedical research companies now refuse to license NIH's patents. This fact undermines the rationale for appropriating so many billions of dollars to fund this basic research. The impact of these price controls has been startling. 1993 was the worst year for new CRADAs in the history of the program. In 1992, 47 new CRADAs were reached and in 1993 this declined to 26 new CRADAs. Moreover, most of these new CRADAs do not involve drug development, a trend that results from the application of the pricing clause.

We believe that S. 1537, if enacted into law, should be interpreted to assume that NIH will receive "reasonable compensation." There is no need to go further. I am confident that BIO would strongly support the legislation if that is how it is interpreted.

Press reports outline a legislative proposal to be offered as amendment to the health care reform legislation which would extend the NIH price control process to all research which has been funded in whole or in part by the Federal government. Any such proposal would be disastrous for the transfer of this technology to private firms. We would encourage the Chairman and this Subcommittee to review any such proposal and oppose it if it is offered to the health care reform legislation. It would be completely inconsistent with the terms and intent of S. 1537. There is no subcommittee of the Congress that would understand better what this amendment would mean to the whole basic research function of the government and the commercialization of this research. Ultimately, as the Chairman so well understands, if this research is not commercialized, it becomes more difficult to justify the appropriations for it.

ENTREPRENEURIAL FINANCIAL POLICY ISSUES

Approximately one percent of the U.S. biotechnology industry is profitable, so very few of our companies have the profit that creates tax liability. They are, however, highly dependent on certain tax incentives, and they can have an important impact on the competitiveness of the U.S. biotechnology industry.

BIO publicly supported enactment of the 1993 budget reconciliation legislation because of the targeted capital gains initiative and the R&D tax credit.

BIO is developing a comprehensive agenda for an Entrepreneurs Tax Incentive Act for the next Congress. We will propose: making the R&D tax credit permanent, amending the R&D credit (to offer greater incentives to start-up firms), amending the capital gains incentives for investors, amending the 'change in ownership' rules for Net Operating Losses, and amending the alternative minimum tax (AMT) to encourage investment in biotechnology firms.

The Financial Accounting Standards Board (FASB), which develops the "generally accepted accounting principles" used by the accounting profession in this country, issued a draft proposal which will require companies to include employee stock options as an expense on their financial statements. The Biotechnology Industry Orga-

[14] Anderson, Christopher, "Rocky Road for Federal Research Inc.", Science, 497 (October 22, 1993).

nization believes that the FASB proposal is misdirected, unnecessary, and harmful to the long-term growth potential of the biotechnology industry.

Biotechnology companies use stock options broadly. A 1992 survey of our association's membership showed that over 70 percent of our companies use stock option and other long-term incentive plans, and that more than 50 percent offer those plans to 100 percent of their employees. These results are consistent with other surveys of smaller and high-technology companies generally. This is a critical issue for our companies.

We support efforts by Senator Joe Lieberman to prevent the implementation of this proposal and to provide incentives for broad-based stock option plans through his Equity Expansion Act (S. 1175), and efforts by Senator Bill Bradley to put the Senate on record in opposition to the FASB proposal, through S. Con. Res 34.

FEDERAL REGULATORY POLICY ISSUES

The biotechnology industry is one of the most heavily regulated industries in America. Our biomedical firms are regulated by the Food and Drug Administration (FDA), our bioagriculture firms are regulated by FDA, the Department of Agriculture (USDA), and the Environmental Protection Agency (EPA), our bioremediation firms are regulated by EPA, and our bioenzyme firms are regulated by FDA and EPA. We accept this regulatory framework because risk assessments are science based.

Our industry has several priorities on regulatory policy each of which can impact on our competitiveness.

FDA Appropriations and User Fees: The biotechnology industry strongly supports increasing appropriations to the FDA and full implementation of the prescription drug user fee legislation at FDA. We supported enactment of the legislation because the proceeds of the user fees have increased the staff levels at FDA and accelerated the product review process under strict performance standards. We are concerned that the proceeds of the user fees may not, in fact, be used for this purpose. We also raise a cautionary note that the Reinventing Government initiative might limit the number of employees or the grade of the employees that FDA may hire. At present, there is a freeze at FDA on new promotions to GS-14 and -15. This has made it extremely difficult for FDA to recruit new medical reviewers, who are key to the review process. If FDA cannot increase their personnel, they will be unable to quickly review new life saving therapeutics. This not only will breach the agreement reached during the framing of the legislation, but will adversely affect those in society that depend on new break through biopharmaceuticals to treat illnesses for which there is no available treatment.

Labeling of Genetically Engineered Foods: From the very beginning it has been the consistent position of the biotechnology industry that government should regulate the products, but not the process. A host of scientific authorities have confirmed that there is no evidence that products produced through genetic engineering present any different or higher risk factors than products produced through conventional means. To treat genetically engineered foods differently, for instance, to insist that they be labeled, would be to imply that there is a problem where no problem exists. If some producers should chose to label their products indicating it has not being genetically engineered, we join FDA in insisting that the labeling used must be truthful, accurate, and not misleading.

Pre-Market Notification: We believe that through the current regulatory scheme, the Federal Government, i.e., USDA, EPA, and/or FDA will be in the possession of essential information about biotechnology foods before they reach the market. Because of the method by which plant products are developed, this information would ordinarily come to USDA or EPA first, but where there has not been public disclosure in the U.S. under applicable USDA and/or EPA regulation, we would then agree that notification should be made to FDA. We object to the necessity of submitting identical data to more than one regulatory agency and would call upon the agencies to observe President Clinton's executive order 12866 of October 4, 1993 which instructs the regulators to avoid promulgation of inconsistent or duplicative regulations.

INTELLECTUAL PROPERTY PROTECTION

Innovation is the hallmark of the biotechnology industry. Patents protect our intellectual property inventions from pirating. Without valid and enforceable patents, the incentive for research will dissipate and our competitiveness will be reduced.

Patent and Trademark Office: The biotechnology industry strongly supports appropriations for the U.S. Patent and Trademark Office (PTO), an agency of the Department of Commerce. Valid and enforceable patent rights are a prerequisite for

success in the biotechnology industry. Because of this, it is essential that the Patent and Trademark Office be provided the funding and resources it needs to properly examine patent applications. We therefore strongly support full appropriation of fees collected by the PTO, and oppose measures that would diminish the PTO's ability to handle the volume of applications that it presently receives. In particular, we oppose diversion or withholding of appropriations of fees collected from patent applicants, for any purpose other than PTO operations. We intend to continue to work closely with the PTO to ensure that its examining operation functions effectively. We currently work closely with the PTO on a whole variety of initiatives, including the Biotechnology Institute, which trains patent examiners in Section 180. We also work closely with the PTO on a variety of substantive issues, including utility claims, experimental use exemptions, and patent harmonization.

Biotechnology Patent Protection Act: We have championed the Biotechnology Patent Protection Act, S. 298 and H.R. 760, bills that would amend our patent law to afford needed additional protection for process inventions, including those in the field of biotechnology.

Under present law, biotechnology companies cannot prevent importation of a product made abroad which uses a material patented in the United States, unless they have patent protection for the process. Although not unique, the field of biotechnology is particularly susceptible to this problem. Take the common example of an inventor who develops a "host cell" through genetic engineering. Such a cell can be used in a biotechnological process to produce a protein which may or may not be patentable. The inventor may obtain a patent on the host cell. However, the steps of the biotechnology process may be, and typically are, conventional apart from the use of that patentable host cell and, under current law, may or may not be patentable.

Under present U.S. patent law, the holder of a patent to the host cell would be able to preclude another from using that cell in the United States to make the protein. However, without patent protection for the process, the inventor has no effective remedy against someone who takes the patented host cell to another country, uses it to produce the protein, and imports the protein back into the United States. See, e.g., *Amgen, Inc.* v. *United States International Trade Commission,* 902 F.2d 1532, 14 USPQ 1734 (Fed. Cir. 1990). Thus, our law currently provides an unfair advantage to unauthorized users abroad of technology patented in the United States.

The legislation would provide an effective means of protecting technology patented in the United States from unfair foreign competition, because it would permit an inventor to obtain patent protection on a method of making or using a product, if that product itself is patentable. Thus, a patent on the method of making a protein by using a host cell would produce a basis for an infringement action under section 271(g) of title 35, United States Code. The patentee could also petition the U.S. International Trade Commission to issue an exclusion order under section 337 of the Tariff Act of 1930.

This legislation has twice been adopted by the Senate and is now pending in the Intellectual Property Subcommittee of the House Judiciary Committee. The Chairman of that Subcommittee, Congressman William Hughes, has pledged to mark up this bill in the next few months and work towards enacting legislation to solve this problem. We look forward to working with him and the Chairman of the Senate Subcommittee on Patents, Copyrights and Trademarks, Senator Dennis DeConcini, to secure adoption of this legislation in this session of the Congress.

Biodiversity Treaty: The Biotechnology Industry Organization urged President Clinton to sign to the Biodiversity Treaty. We urge the Senate to ratify the treaty and confirm the Administration's interpretative statement which ensures adequate protection of intellectual property. While there must be adequate recognition of the value of the products of nature, recognition must also be given to the contribution made by individuals and institutions in modifying these products to make them useful to mankind. We believe strongly that the value of biological materials is enhanced when intellectual property rights are created, protected, and enforced by all nations. We believe that it is absolutely essential that the Biodiversity Treaty be interpreted in accordance to this precept. Moreover, the value of biological resources and the likelihood of greater conservation efforts is enhanced by stronger intellectual property protection in the modifications made by our industry.

INTERNATIONAL TRADE ISSUES

BIO is strongly in favor of free trade. This is a competitive industry, our products will be in demand in international markets, and we hope to be a major exporting industry.

BIO supported NAFTA and the implementing legislation.

We support the recently concluded Uruguay Round of the General Agreement of Tariff and Trade (GATT). We will benefit if the United States Congress enacts implementing legislation for the GATT Round.

Specifically, biotechnology benefits in two fundamental ways from the GATT Round. First, the virtual elimination of tariffs in the pharmaceutical sector makes many of our companies better able to compete fairly in international commerce. Second, we hope to benefit from the improvements in the Trade Related Intellectual Property measure (TRIPS) provisions of the Round. The strengthened patent protection and internationally delineated standards of adequate and effective intellectual property will help avoid piracy.[15]

BIO's principal interest in trade issues is the protection afforded to the intellectual property of U.S. biotechnology firms. As the world leader in biotechnology, foreign firms have an interest in delaying legislation that would provide adequate protection to intellectual property developed in America. We must insist on adequate protection in all of our bilateral and multilateral negotiations with our trading partners.

HEALTH CARE REFORM ISSUES

I understand that a witness on the second panel will discuss the biomedical sector of the biotechnology industry and cover the impact of the health care reform legislation on the biotechnology industry. Let me just say that BIO strongly supports universal coverage, a prescription drug benefit for Medicare beneficiaries and reliance on market forces to contain costs. For the same reasons that we oppose price controls on NIH CRADAs, we oppose the imposition of direct or indirect price controls on breakthrough and new medicines. Such controls would provide a disincentive for biomedical research and adversely impact on competitiveness.

OUR NATION'S ECONOMIC FUTURE

America's biotechnology industry is critical to our Nation's economic future. This industry currently employs over 100,000 Americans in high wage/high skill jobs, makes major contributions to our health and welfare and deserves strong, bipartisan Congressional support.

Technology policy is more than the sum of a series individual, isolated individual Legislative and Executive Branch initiatives. The biotechnology industry needs greater understanding from policy makers of its strengths, weaknesses and needs. More focused attention on a comprehensive biotechnology strategy is required. We are a very heavily regulated industry and we must be sure that policies in one sector do not undermine policies in another.

Infrastructure and capital needs for biotechnology are profound.Unlike other industries that need more roads and bridges, or fiber optics and transponders, the biotechnology industry needs basic scientific research, access to capital and coherent government regulation.

Biotechnology in the United States is substantially ahead of our other trading partners because of the government/private sector partnership in funding basic science research, especially at the National Institutes of Health; relatively free access to capital from venture capital to equity markets; and an entrepreneurial environment and culture that accepts risks.

The three most important actions Congress can take to further the interests of the biotechnology industry are:

(1) to strengthen R&D (e.g. adequate funds for NIH, and a permanent, reconfigured R&D credit);

(2) tax and fiscal policy that facilitates access to capital (e.g. improved capital gains, and reversal of the proposed FASB treatment of stock options); and

(3) government regulations that fairly address risk and permit markets to function effectively including section of proposed bans on genetically produced products and reliance on mature market forces to set reimbursement levels for innovative products.

Thank you very much for the opportunity to testify. I am happy to answer your questions.

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[15] BIO has been concerned about issues in the GATT negotiations, including the proposed Dunkel text subsidies code, which would have created rights of action against major U.S. technology support and transfer programs. The draft would have set notification requirements that would have forced disclosure of competitive strategy and trade secrets. The Administration has informed us that this draft was modified to alleviate these concerns.

Senator ROCKEFELLER. Senator Burns, before I turn to you for any comments you might have, believe me, I took care of Montana. I mean, people were pulling their handkerchiefs out and weeping. We had to get control of the audience. [Laughter.]

This is going to sound sort of silly. I do not want you to laugh at this, but I am going to make two analogies, and the first one you will laugh at, to this whole question of the Federal Government and the interrelationship with pharmaceuticals, biotechnology, and the nervousness that biotechnology and pharmaceuticals had with the Government even as billions of research money has come in over the years.

The first thing, we just went through an instance yesterday, or this morning, when the Fed yesterday raised its short-term discount rate by whatever it was, one-quarter of 1 percent, and the market discounted it, and the market discounted it because the market already knew it was going to happen because President Clinton and Alan Greenspan had gone to the White House and they had talked, and everybody had speculated. They said, I guess there is going to be—and so, in other words, the perception there was not any problem.

Now, had that just happened, the stock market probably would have dropped by 50 points, if it had just happened. But because there was—people sort of understood it, the perception was entirely different.

Now, this is the part which is embarrassing to say, but it needs to be said. Back in the fifties, when President Eisenhower was President, he had a heart attack, and of course, that was devastating to the Nation. When President Eisenhower had a bowel movement, which was considered a strong indication of recovery, the stock market went way up.

Now, all I am trying to say to you is that this business of perception really is important, but I think there is an equal responsibility on the part of the pharmaceutical industry and the biotechnology industry to, when they see words like—what was it, "the appropriate price"?

Dr. GREENWOOD. Reasonable price.

Senator ROCKEFELLER. And then the whole business of CRADA's, which are going down all of a sudden, and then the business of the breakthrough drugs which we talked about on pharmaceuticals, I cannot imagine a health care plan in which the Government would try to discourage breakthrough technologies in that breakthrough technologies are the greatest costsaving. That is the greatest costsaving you could do in health care. It is like doing preventive medicine on everybody for 20 years. I mean, it is just extraordinary.

But the pharmaceutical industry perceives a threat because there is something called a breakthrough drug price commission which reviews—yet cannot set policy. You use the word "price controls." They cannot set the price—by law, they cannot do it. All they can do is look at the price and comment on the price, and maybe that will get removed.

But the perception, therefore, is that the Government is against the necessary research dollars, the necessary time, or is against the

pharmaceutical industry putting the money into what is so clearly in our benefit to happen, and that is what mystifies me.

Industry and Government have been interlocked. Biotechnology could not have taken off without the U.S. Government. Senator Burns and I spent all these hours on the floor last week, in the Senate arguing against people who were screaming about industrial policy, and here we are talking about a major impact of Government money which allows these industries to get going.

So, I do not know—it is just philosophically perplexing to me, because health care—the cost of health care is going crazy. We have a fiduciary responsibility to the public. The pharmaceutical industry has been doing well. We have the figures here somewhere. It has been doing fairly well, and we expect it to continue to.

The health care bill is expected to increase activity and possibilities. More people will be covered, so there is more focus on health care, more interest, much more national awareness, individual sensitivity to the problems of health care, therefore more interest in breakthrough possibilities, but still, the pharmaceutical industry looks upon this as market-depressing, "I cannot get capital, no venture capital, no bank will loan to me, I cannot go to the public markets and get money," and that perplexes me. That is all I am saying.

It just perplexes me, because I know that is not our intent, but that is clearly your perception, and we cannot abandon our fiduciary responsibility in terms of health care, because I mean, "breakthrough," by definition, means that when it is achieved there is a period of time when it is exclusive, when you have exclusivity in the market, which ought to be a profitable period. You are talking prior to that time when you are trying to raise the research so you can get to that point.

We have a fiduciary responsibility. That is why Conrad Burns and Jay Rockefeller voted to cut the budget deficit by $500 billion, and we will probably do more, so—there is this crisis, and we have to get control, so sort of talk to me on that. We have a close relationship in history, but now everybody gets very nervous. Just talk to me a little bit about that.

Ms. CONTE. I would love to comment on that. Two things you brought up. One, you recognize, and that is why I feel this collaboration has been working between Government and industry, that breakthrough drugs can have one of the greatest impacts on the total cost of the health care system because they can provide alternatives to surgery or long-term care situations, and many other alternatives that are being used out there now in the health care system.

The breakthrough drug review board just focuses on the cost of a breakthrough drug. And if you talk about your fiduciary responsibility, that is such a minuscule portion of the total health care bill. It is less than one-fifth of 1 percent. Yet, look at the dramatic impact it can have on the cost of the total health care industry.

So, this board, which is decreasing the opportunity to create these breakthrough drugs, is therefore having the impact of not allowing many of these other decreases to occur by coming up with other answers.

Senator ROCKEFELLER. But why? Who says? I mean, you are making the assumption. If the biotechnology firms perpetuate the perception of price controls, if they do, will this not be a self-fulfilling prophecy? I mean, this review board cannot set price. They can only comment on price and that is all they can do.

And then, yes, the HHS Secretary can say that price is so outrageous that we will not reimburse it. But that in a sense is an ultimate exercise of fiduciary responsibility. I cannot imagine it is being exercised in any kind of breakthrough biotechnology or pharmaceutical technology which cures the kinds of things that you are working on.

Ms. CONTE. Why look at the price in isolation? Why not look at outcomes?

Senator ROCKEFELLER. I suggested that.

Ms. CONTE. That is what we like.

Senator ROCKEFELLER. To Eli Lilly, I said that we should put that in the legislation, that outcomes should be part of the analysis.

Ms. CONTE. And why not put it in a body that is already set up or that is already existing, the AHCPR which is already an up-and-running organization, and charged with doing outcomes research. And provide information to the market out there and let market forces control whether a breakthrough drug's price is reasonable relative to what the alternatives are and, therefore, keep the incentive for more products to follow through which is going to give the market forces greater strength in reducing the price ultimately long term.

Senator ROCKEFELLER. We could do that. We could put it in the AHCPR. It was created in 1989 in the RBRBS legislation, and nobody pays much attention to it. I mean, it is doing its work very quietly, very systematically. You know, it is slowly taking various procedures, but it is something nobody pays much attention to.

It is terribly important. Outcomes research is the most important thing we can do in health care it seems to me.

Anyway, I will back off and let Conrad Burns say more intelligent things.

Senator BURNS. Thank you, Mr. Chairman. Let me apologize for showing up late. We have got two or three things, too many fish in the fire I think, to get it all covered today.

I want to ask a favor of both of you. Can I submit my questions to you in writing and have you respond to the committee and to myself and to the chairman? We are cranking on an airplane leaving town, and one of the witnesses is to testify today, and I am wondering if we cannot do that. Is that possible, and I just ask permission to put my statement in the record?

[The prepared statement of Senator Burns follows:]

PREPARED STATEMENT OF SENATOR BURNS

Chairman Rockefeller, I want to thank you for agreeing to hold this hearing on a segment of our scientific research that I personally think is vital to our ability to feed, clothe, and house our Nation's 260 million people in a wholesome and healthy way.

It is my view that biotechnology has a tremendous potential to improve the quality of our lives and generate new jobs. Already, biotechnological breakthroughs have produced new ways to prevent and cure disease, develop better crops and livestock, and protect the environment.

Biotechnology is a rapidly expanding industry that may play a prominent role in the U.S. economy by the end of the decade. Worldwide annual sales of biotechnology-derived products have grown from zero in 1980 to $5.9 billion in 1992 to $7.0 billion by 1993. By the year 2000, such sales are projected to reach $50 billion.

In Montana, biotechnology is the newest and fastest growing industry with companies springing up in places like Bozeman, Great Falls, and Polson. Similarly, the number of biotechnology companies—mostly small businesses nationwide—have jumped from 93 companies before 1970 to over 1,000 companies today.

It takes 10 to 12 years to research, develop, and bring a biotechnology product to market at an average cost of $259 million per product. In fact, the average biotechnology company incurs total expenses between $300 and $500 million before any operating revenues are earned on a product.

Early-stage financing typically is raised from venture capital companies, institutions, and individuals. As the product approaches the commercialization state, and requires much more capital, the companies usually turn to public stock offerings to raise money.

The industry is extremely concerned, as I am sure Lisa Conte from Shaman Pharmaceuticals and Mark Skaletsky from GelTex will share with us, that possible price controls on biotechnology products in the Clinton health care plan may discourage potential investors in biotechnology ventures.

An area of particular interest to me are the agricultural applications of biotechnology. American agriculture is the envy of the world. Last fall, I had a group of Russian journalists spend the day with me and the thing they were most impressed with was the breakfast selection in the Senate dining room.

Because American farmers, ranchers, and foresters have rapidly incorporated the newest technologies including biotechnology into their operations our Nation has the highest quality, most plentiful, safest, and inexpensive food, fiber, and housing in the world.

By using bioengineered products to speed animal growth, improve feed efficiency, and produce leaner meat, American consumers have the luxury of dining out at restaurants with menus featuring a variety of beef, lamb, pork, and poultry selections.

I am pleased Montana State University's dean of the College of Agriculture and Director of the Agricultural Experiment Station Barry Jacobsen is joining us today on the second panel to talk about agriculture use of biotechnology. MSU is one of the Nation's leading land grant universities in the area of biotechnology research.

One of the projects we will talk about later is the unique biological control of leafy spurge MSU is doing at the USDA Northern Plains Soil and Water Research Center at Sidney, MT. Leafy spurge is a weed that causes an estimated $100 million economic loss in a four-State region including Montana. The biological control of leafy spurge could also drastically reduce current reliance on chemical weed control for leafy spurge and protect the Yellowstone-Missouri-Mississippi River system from potential pollutants.

On the environmental side, the work currently underway in Butte, MT, with the MSE Mine Waste Technology Program is on the cutting edge of biotechnology mine waste remediation in the United States.

By using microbes or bacteria to reclaim toxic and precious metal from the Berkeley Pit biotechnology could make the world's largest superfund site a potential win-win for that area of Montana.

As we can see, there are a number of opportunities for biotechnology to help improve the world in which we live. Only if we listen to the naysayers and individuals with hidden agendas will we limit the future benefits our society can gain from this vital new industry.

I look forward to hearing the witnesses today and once again thank my good friend from West Virginia for holding this hearing.

Senator ROCKEFELLER. You are saying one of the witnesses has a plane problem?

Senator BURNS. Yes. Dr. Greenwood, biotechnology—I will say why my interest first of all in my statement is very acute in this area. I have just come from a hearing over in the U.S. Forest Service where dollars and dollars become less and less in the management of our national forests. And I also understand—and when we talk about biotechnology or biochemistry it applies to the health of human beings but it also applies to health to our animals and health to our plants. It applies to every living thing.

And where I went up and walked through an area—now weeds, when you talk about weeds it is not one of those great, sexy issues that make headlines in the Washington Post, but it does in the Ravalli County Republic because it is a situation—when we start talking about production agriculture we have to deal with that.

And we are also living in a world where chemicals are becoming less and less used and desirable for the control of weeds. So, with the development in biochemistry and how we control those weeds, where we spend up to $1,500 an acre on the Forest Service of your tax money and we are losing the fight as they continue to spread. And if they spread on public lands, they come on private lands.

Now, we do cannot afford $1,500 an acre to control something that will take us out of the business of producing food and fiber for this society. So, Dr. Greenwood I would ask you the Clinton administration's position on the direction for the use of biotechnology? What direction should we take in this country?

Dr. GREENWOOD. Well, thank you, Senator, and the beautiful State of Montana, as I know well, does have one of the most beautiful forests, and I would certainly hate to see the weeds taking over.

The biotechnology effort in weed science and in agricultural areas is increasingly important, and it is going to play a role in the future not only of our forests, but also as you said in environmental remediation and a variety of other areas that have to do with decreasing pesticide use and improving our food and fiber production into the 21st century.

One of the things that the Biotechnology Research Subcommittee, which is now a subcommittee of the Fundamental Science Committee of the National Science and Technology Council, which I reviewed briefly before you were able to join us, one of the things they are addressing is what are the opportunities in the areas of biotechnology along with the health opportunities, but the other areas.

And the environmental and the agricultural area are prominently displayed in a report they are working on that will be released in the not too distant future, and which will help us to shape the programs and policies we need as we enlarge the Nation's investment in the research base that is relative to the problems that you cited.

So, I think that you can expect, and I think that the industry itself would expect to see substantial growth and development in the areas related to animal health, food and fiber production, pesticide and weed controls. These are obviously very important areas for development, and they should represent an increasing market share, and probably overall an increasing effort as we develop our environmental policies and our agriculture, food and fiber policies.

There is also another committee of the NSTC called Health, Safety, and Food, and this is a committee which will be working rather intensely on food safety and on programs that would enhance our competitiveness in food and fiber production, and in decreased pesticide and chemical use.

Senator BURNS. It is my understanding, and I need some help from you, and you can take the message back, but the President's budget proposes to cut nearly $800,000 for funding for bio-

technology research in the North Plains Soil and Water Research Station in Sydney, MT, while funding $2.6 million for the European Biological Control Laboratory in Montpelier, France.

At this particular place we are not only going into an area—this is irrigated agriculture in the lower Yellowstone Valley. We are going to redo a Clean Water Act of which we will be a part of—nonpoint source pollution will be a part of that testing of waters, and how do we deal with the contamination of ground waters and this type thing.

I would ask you, does that make sense to you? I think it is a terrible injustice on the people that we are doing business and working for here in this parcel. I am asking you to kind of help me out there, if you would.

Dr. GREENWOOD. Senator, I am going to have to confess that I do not know the details of either one of those programs, but I will be very happy to get back to you in writing.

Senator BURNS. And I know you would, and that is sort of unfair, but I need your help.

Dr. GREENWOOD. I would be happy to do that.

Senator BURNS. OK. Ms. Conte, I understand you are a neighbor.

Senator ROCKEFELLER. He is worth it, Dr. Greenwood. [Laughter.]

Senator BURNS. I just have a question for you real quickly—59 percent of the new funds going into the marketplace, into seed and second-stage-type companies, if venture capitalists continue to fund new ventures and not support existing ventures, what do you see happening to our R&D in this country, research and development?

Ms. CONTE. Venture capitalists—it is not a tradeoff of supporting existing venture versus starting new ventures. They cannot support the existing ventures. I am a venture capital-started company, venture capital funded company. Venture capital is my past. They can no longer afford to fund my company. I have 100 employees. My valuation is way too high for the types of returns that they are looking for. So, their only alternative is to continue to fund new companies. That is all they do.

The problem comes in the financing, the mezzanine financing and the public financing thereafter, and that is the money that is drying up, and that is the money—if this problem does not get resolved in a short period of time there will be a very large number of companies that will cease to exist in the current form that they are in and will have to become the arms of a major pharmaceutical company, or would have to sell out overseas. Some say they might merge. This is a classic example of two plus two equals negative one. We both have the same needs if we merge, which is cash. So, that is where the problem is.

Venture capital as far as I see and I know will just continue to roll along as a successful industry because of the entrepreneurial environment here in the United States.

Senator BURNS. Thank you, and I will have some questions for you. I understand that we are going to be neighbors or we are neighbors?

Ms. CONTE. We are in Big Sky.

Senator BURNS. How about that. It is snowing today, by the way, up there.

I want to thank the chairman and I want to thank this panel. And, again, I want apologize because I was late, but thank you very much.

Ms. CONTE. Thank you.

Senator ROCKEFELLER. Thank you, Senator Burns. Dr. Greenwood, could you go over areas where you think in biotechnology that we are doing better as a country, and other areas where, for example, the Japanese or the Taiwanese or the Koreans or French or others might be doing better? Where do we appear to be weak and strong?

Dr. GREENWOOD. I think the best answer to that is that the U.S. biotechnology industries as a group clearly have the global competitive edge. It is very apparent in the pharmaceutical area and the health-related area. In fact, there was a Washington Fax report today that you may or may not have seen which was on a study released by the European Union concluding that the U.S. pharmaceutical industry leads their European counterparts in Europe.

In Europe, 65 percent of the biotechnology patents are from the United States. Only 15 percent are European, and only about 13 percent are Japanese. So, certainly the United States has a strong competitive lead in several of the important global markets, the European global market being one.

In some of the areas that Senator Burns brought up, environment remediation, some of the agro-chemical-biotechnology areas there is some evidence that some of the European companies and some of the Japanese companies are aggressively developing products in that area. But to my knowledge, we do not have any reason to believe that they have as yet developed a competitive edge to substantially challenge the U.S. edge.

I think the big issue here is that there are policies in place, developing in the Pacific Rim countries and to some extent, as I understand it, in the European Community, that aggressively encourage the development of the biotechnology industry in those countries. And so while they may not have the competitive edge now, there is reason to believe that we should ensure the healthy competitiveness of our industry in order to maintain the position that we currently are in the enviable position of having.

We have focused very much on the health-related biotechnology industry. This is at least in part because of the history of the discoveries of the biotechnology process and then its applications in health-related areas. And there have been some stupendous successes. And, as you just heard from Ms. Conte, there are likely to be a number more over the next few years.

It is a dramatically new way of moving drugs from conception through the clinical testing process with timeframes such as the one she just described which are very startling to those of us who have spent time, at least in my past career, working in the more traditional pharmaceutical industries and with their background.

I would just hope that we can continue to work with the industry and that we will continue to work with the industry in such a way as to ensure this competitiveness does not get sapped away as other countries see what we already know to be the case, which is the tremendous benefit for the future and the opportunities to open

a whole new set of jobs in a high-technology industry, which is also a clean high-technology industry.

Senator ROCKEFELLER. Ms. Conte, I am going to ask you exactly the same question after I ask Dr. Greenwood one more question, so you just be thinking about how you want to answer that.

A couple of business people have told me that they spend in biotechnology hundreds of millions of dollars, and years and years and years and years to develop a product, and that it has gotten now so the FDA is taking sometimes up to 4 years to approve what they have spent this time doing.

Now, those rules do not apply in other countries, so that the prospect of a U.S. biotechnology firm not wanting to wait around for FDA to make its judgment, and to take their production or their research or some combination thereof to the other country where they can just start immediately, because they do not have to worry about the 4-year wait, and the whole implication of that in our future, do you see that as serious? Do you see that as something that just somebody happened to tell me but is not particularly true or what?

Dr. GREENWOOD. Well, I think that is a threat not just to the biotechnology industry but to other industries as well, that where we have regulatory processes in place which are different from other countries, there is always the temptation of the industry to move to a less regulatory, constrained environment and to develop products.

I think as we move into a more globally competitive environment we are going to see a lot of countries doing this, looking for the friendliest place to move into some of the development phase. And in some cases we will be the friendly environment and in some cases other countries may be more attractive.

It is regrettable if that moves jobs and moves opportunities for our citizens out of this country, and I think that is the biggest danger and the one we need to be monitoring carefully and to be concerned about.

Senator ROCKEFELLER. Are we seeing some of that today?

Dr. GREENWOOD. Well, certainly it is the case that in traditional pharmaceuticals there have been a number of products developed in the European market prior to their being developed in the U.S. market with certainly some attribution to our regulatory process and the time and delay with the FDA.

As you know, there has been some real effort in this administration to decrease the FDA review process, and with the new user fees Dr. Kessler has certainly been on record that he believes it will be possible to reduce the review at least of some fast-track drugs more in the range of 6 to 18 months rather than the current, as I understand it, 2½ to 4 years, depending on the type of drug.

So, I think we are making some progress in trying to make our regulatory review times shorter. But I also think there are sometimes reasons why drugs, pharmaceuticals in particular are tried in other countries, and there are reasons that we do not let them into our market that do have to do with the health and safety of our population.

And so we are dealing with a tradeoff here between the important regulatory effort that we make and ensuring the safety of

these drugs for our population, and the opportunity to develop them and create jobs. It is, as you know better than anyone, a tension that will continue to exist as we move forward, especially with some of these very risky drugs that we are being continually pressed to put on the market in a shorter and shorter time.

Senator ROCKEFELLER. Ms. Conte, you can comment on that, too, if you want.

Ms. CONTE. I think there is no doubt that clearly the United States is the current leader in the biotechnology industry and all aspects of it: health care, agriculture, any other applications of it. This also, unfortunately, means that it has become the target of the rest of the world, and this includes—and I work in all different parts of the world, the North and the South, the developed and the developing countries. It is a target. The biotechnology industry is a target.

In particular, Japan is one country that you can single out. My experience, both with the Japanese and the Europeans, has been how are they going to go about developing a biotechnology industry and gaining the economic and societal value of this industry? They are going to buy it. And I will tell you two stories that support that.

The Japanese, recognizing the tie between return on investment for products and incentive to do research, reimburses breakthrough products at sometimes three times the level that we have here in the United States. There is no product—I believe that is true. I should check that. There is no breakthrough product that is priced lower in Japan than here. And they have specifically done that to generate more research into breakthrough products and therefore foster the creation of a stronger biotechnology industry there.

European pharmaceutical firms: I am in discussions with them all the time for potential licenses to my products or investment. I was talking to the CEO of a major German firm, who has decided by the way to move his headquarters from Germany to Connecticut because of the detrimental effect on research and innovation in that country when they instituted price controls several years ago, and I asked him what he thought about the whole situation with the valuation of young emerging biotechnology pharmaceutical companies in the United States, and his answer—his English was not great, but his answer got through, which was "I am walking around with a shopping bag, and he is just going to buy up the technology." And that is how they are going to be able to catch up.

All the risk capital that was put in, all the transfer from the Government, all the venture capital to fund this, is at risk of being bought up by other countries that recognize it as an opportunity because we cannot access the capital right now, the critically needed capital, to take these things through development.

Senator ROCKEFELLER. You are facing from the Japanese what they call cross-licensing? In other words, you need the money, they know that, you have got the patents, you have got the technology, so they say we will give you the money, make you solve it, and you give us the technology.

Ms. CONTE. The technology we have in hand, and teach us how.

Senator ROCKEFELLER. And that, in some ways, has been the history of the Japanese industrial revolution since the end of the Second World War; has it not?

Ms. CONTE. Absolutely.

Senator ROCKEFELLER. Cross-licensing. They do that with the Patent Office. They hold things up with the Patent Office, and then they come and they say "OK, you are having trouble with the Patent Office. We will give you the money, you give us your technology."

Ms. CONTE. They do not recognize the coverage that we have in our patents here, so you think you have patent coverage in Japan but in fact your technology gets changed slightly and utilized in a way that it would still be protected here.

Senator ROCKEFELLER. Senator Burns' witness has a plane to catch. I want to ask each of you to sort of stretch your minds, and I want to get out from under breakthrough drug commissions.

Ms. CONTE. You brought it up. [Laughter.]

Senator ROCKEFELLER. I want to get out of that for a moment and just say if things worked right, what do you foresee the nature of the explosion? Just let your mind wander, both of you, in this field, in this country. What can happen?

Dr. GREENWOOD. I will be happy to take a crack at that. I think the biotechnology industries represent for this country a new type of industrial revolution. I think we will see the processes and the products developed from the biotechnology industry as critically important to the next 50 years for the country in terms of job creation and in terms of the products.

The ability, particularly, to develop very targeted, very clean, very specific products, especially with respect to some of our concerns with the environment and elsewhere, are going to provide us with a whole new way of looking at how we manage our resources, how we manage our health, and how we look at the future of our children. And so I think it is a critically important set of industries.

And I think it is poised in a way, and it is such an excellent example of the kind of pioneering spirit that this country has had and the kind of creative intellect that we have nurtured with the funding that we have given, that this Government has given to researchers, has led us to a whole new way of looking at life and a whole new way of looking at product development.

I think that is probably not nearly as well appreciated in this country as it might be if we had a more scientifically literate population and people truly understood the revolutionary basis of this industry, and that is, perhaps, one of the reasons why this administration and those of us who have come to serve it find the challenges of the problems and the opportunities of this set of industries so interesting right now and so important to talk about and address. So, I want to thank you again for holding this hearing.

I hope that answers this question. I would like to be able to say I know these are the 93 products that will be on the markets and these are the diseases that will be cured, but it is these technologies that will allow us to really transform the lives of some very sick children and to solve some very important global problems in clean, healthy, ways.

Senator ROCKEFELLER. Ms. Conte.

Ms. CONTE. To look at whole new ways of practicing medicine. My brother who is a surgeon, God bless his soul, I would hope that this would be considered ancient technology in the next 10 years, and he is a cancer surgeon, as we come up with new ways to treat that.

I think the effect on the economy—this is jobs of the future, this is what we talked about with NAFTA, these are high-wage, highly skilled, high-trained jobs, but as the industry develops we are also pulling along the minimum wage worker as you are going to create manufacturing jobs. And so the industry will have an impact on much more than just the small population of the economy right now.

And after that, I am going to say the environment. And I say after that because the first thing that we have to do is take care of people. We have to work in the worldwide economy, the worldwide standard of care. And if you do not take care people first you are not going to be able to take care of the environment, and that is a critical piece of this whole thing.

And with the environment, along with that will come human rights issues around the world.

So, I think the impact worldwide is limitless, but I think it takes time and I think, as I mentioned, the implications from simple policies now I do not think we are necessarily realizing the side effects, the fallout, because we are talking about such a long-term industry that requires so much up-front risk capital.

And I would also like to thank you very much for the opportunity of speaking today.

Senator ROCKEFELLER. Well, you have both been terrific, and I just wish everybody in the world was as good as both of you, public sector and private sector. I really thank you both very, very much.

Dr. GREENWOOD. Thank you, Senator.

Ms. CONTE. Thank you.

Senator ROCKEFELLER. Our second panel is Dr. Barry Jacobsen, who is dean of the College of Agriculture at Montana State University in Bozeman; Dr. J. Peter Perez who is president and chief financial officer, Environmental Remediation, Baton Rouge, LA; and Mr. Mark Skaletsky who is president and chief executive officer of GelTex Pharmaceuticals, Lexington, MA.

Dr. Jacobsen, let us start with you because we do not want you to miss your plane.

STATEMENT OF DR. BARRY JACOBSEN, DEAN, COLLEGE OF AGRICULTURE, MONTANA STATE UNIVERSITY—BOZEMAN

Dr. JACOBSEN. Thank you, Chairman Rockefeller and Senator Burns.

The production, processing, and marketing of food employs roughly one in every five people in the United States and accounts for roughly 19 percent of the gross domestic product.

Senator ROCKEFELLER. Could you say that again?

Dr. JACOBSEN. I said the production, processing, and marketing of food employs roughly one in every five people in this United States. It accounts for roughly 19 percent of the gross domestic product. This last year, it accounted for some $42 billion in export surplus for this country.

Biotechnology has impacted this industry for nearly a century, if one considers the traditional plant and animal breeding, tissue culture, and fermentation research. However, with the advent of modern molecular biological techniques, I predict that this technology, biotechnology, is going to have an impact on agriculture similar to what we saw with the impact of modern fertilizers, hybrid crops, and pesticides in the 1940's, 1950's, and 1960's.

It is very clear to me that we need this increase in efficiency that is going to be achieved through biotechnology as the world becomes a free trading environment. GATT and NAFTA have clearly shown us that the low-cost producer is going to have the market.

Now Americans, farmers, ranchers, others employed in this industry, rural communities, are dependent on foreign markets for our agricultural products, absolutely dependent on them. If we are not the low-cost producer we simply will not have those markets. I think biotechnology offers us the ability to improve our plants in terms of yield, their pest resistance, their environmental tolerance, and also to produce very unique products that really offer us an increased potential for added value processing crops here in the United States.

I might suggest to you that I feel in the next few years we will take crops such as barley, and the food production element of barley production will be relatively small compared to the production of biochemicals such as enzymes or perhaps even pharmaceuticals. They have developed a new term for this: "pharming," with a "ph" instead of an "f."

Biotechnology really affords us tremendous potential in the area of crop protection. As you know, the administration has set a goal that they are going to have 75 percent of our production under integrated pest management in the next couple of years. I would maintain with the lesser availability of pesticides and the public concern about pesticide residues, the importance of biotechnology and developing biological controls and biopesticides is ever greater.

The potential to remarkably modify plant genetic material to give resistance to virus diseases that we have never been able to control, or control bacterial or fungal diseases for which we now use pesticides, or control insects in all manner of ways, either through genetic modification or biocontrol, are absolutely tremendous. We now have an opportunity to reduce our synthetic chemical pesticide inputs and replace them with natural biological products.

I think very critical to the plant side of biotechnology is the Plant Variety Protection Act. Therein lies the protection for entrepreneurs to develop new varieties and be able to protect that technology. The U.S. Congress will be considering some elements of the Plant Variety Protection Act this year that is absolutely critical to maintaining competitiveness in this area.

Another area is in the area of animal improvement. Certainly, improved efficiency in animal production is something that we are interested in; perhaps animal fats that contain different kinds of fatty acids so we do not have real or imagined cholesterol problems, the production of vaccines to prevent diseases, the ability to detect microorganisms that might cause food safety problems, are certainly all within the realm of possibility from biotechnology.

I might point out a very clear area where biotechnology has already had a great impact in the animal industry. We routinely now transplant embryos. We can sex sperm, we can sex embryos, and we can even take those embryos and divide them in one-half or in one-thirds or in one-fourths to produce identical twins, triplets, or quadruplets. I think you can see that very quickly you can build up a very superior genetic base in your animal production in this way.

Certainly, the term "pharming" can be used with animals. It has now been very clearly shown that we can modify the genetic composition of animals to produce vaccines, drugs, pharming, if you wish, with animals. It is very easy to see right now under the proper environment where 10 dairy cows could be more valuable than 1,000 are today.

The other area, I think, that we should pay a great deal of attention to is the potential for bioprocessing. We can now modify microorganisms or modify plant materials to produce new and valuable products from a renewable resource, many of which will replace petrochemicals or other resources that are in somewhat short supply. I think as we look at bioprocessing, the opportunity to produce unique enzymes, flavor enhancers, texture modifiers, is going to absolutely revolutionize the food processing industry. And certainly, the very rapid biotests that can be developed through DNA probes and other things will rapidly modify our food safety environment.

Agricultural biotechnology was about 9 percent of this $7 billion industry this last year. This $630 million business has grown by 48 percent in 1 year, one of the fastest growing segments of biotechnology. I think this industry was very much hyped by scientists and venture capitalists in the past decade regarding all the things it could do. I think the reality of actually doing them in the regulatory environment of today has brought some soberness to that hype.

However, now this industry is delivering pest resistant crops, biocontrols—biopesticides, if you wish—diagnostic tests, vaccines, enzymes, and other additives, natural additives that will be used in the food processing industry. I think the continued growth of the agricultural biotechnology industry is dependent on four things:

A stable, predictable regulatory environment. The rules seem to keep changing, and scientists and business people have difficulty keeping up with that.

The second is public acceptance of biotechnology products. We have seen recently the tremendous public debate over BST in milk. That is going to be a barrier, and is something that we have to deal with in terms of public education. Third, I think we must continue the private and public sector research investment.

I might say, Senator Rockefeller, probably for every dollar that the Federal Government has put into biotechnology research, the State governments have probably put in $2. So, we have had a very good State-Federal partnership, along with the private sector.

I think, fourth, and this I do not want to downplay, is the availability of trained scientists. And right now we have enough Ph.D. scientists, I believe. But we are going to need bioprocess engineers, engineers that understand chemical engineering, if you would, in natural systems.

And, last, technical people to work in this biotechnology area.

I might make the relationship to the computer industry. As soon as we found out about the silicon chip you could not find enough electrical engineers. And to this very day that is a ticket to a good job. I maintain people trained in biotechnology are right at that edge right now. We are going to need to pay some attention not only to training the high-powered scientist but to the technical people that will work in the commercialization of this industry.

If these items are cared for, the biotechnology industry in agriculture will improve our competitiveness of U.S.-produced crop and animal products in international markets. It will help our balance of trade.

I believe very clearly it is going to increase the processing of commodities, adding value, if you wish, for U.S. crops that are protected by our Plant Variety Protection Act and our U.S. patent laws both, for food and industrial purposes. It is going to clearly decrease our dependence on nonrenewable resources as we substitute the renewable resources that biotechnology allows us to access.

It is going to, last, improve the profitability of agriculture, giving consumers at the same time a more reliable—less problems with pests or environmental problems—low cost, because we are going to be more efficient; higher quality, because we can now adjust starch, protein, amino acid, nutritional levels in our foods, perhaps keeping them fresh in the markets such as the FlavrSavr tomato; giving them that high-quality, low-cost food supply that so characterizes the United States.

I think we are going to see a lot of small to midsized companies developing not only these new plant varieties or biocontrols but also diagnostic tests, vaccines, biopesticides, et cetera. It is going to create a lot of new highly technical jobs in this country. Most of these will be small to midsized businesses which create the majority of employment in this country.

Agricultural biotechnology, in terms of U.S. competitiveness, I think we are in the lead, with one exception: biocontrol. I think other countries: Taiwan, and certainly through the European continent, if they have not caught up they are very near to doing so.

I will be happy to answer any questions you might have.

[The prepared statement of Dr. Jacobsen follows:]

PREPARED STATEMENT OF DR. BARRY JACOBSEN

Biotechnology is a collection of techniques, both old and new that allows man to exploit basic life processes. These techniques can be used to enhance productivity and usefulness of existing life forms, or produce unique new products from living organisms. Biotechnology may involve new procedures such as genetic engineering, basic molecular biology, as well as more classical tools such as plant or animal breeding, tissue or cell culture, or fermentation. Perhaps the unique thing about biotechnology is that it can be done almost anywhere, and the techniques are generally not limited by geographic location. Potentially, this technology offers opportunities in both rural and urban economic revitalization based on renewable resources. The promises of biotechnology so hyped in the last decade are now beginning to provide improved crops, better pest control, new agricultural products, and renewable sources of basic industrial supplies and even pharmaceuticals. To date, incomplete research, a restrictive regulatory environment, and incomplete public understanding have slowed die development of a profitable agricultural biotechnology-based industry.

Applications of biotechnology in agriculture can be divided into three basic areas: improved plants, improved animals, and the industrial sector via bioprocessing. The production and processing of food, and ultimately its marketing, employs approximately one in five people in the United States today. This basic industry area is a fertile place for the application of biotechnology and will have dramatic implications for U.S. competitiveness in the world. Applications in agriculture provide entrepreneurial opportunities because of the legal basis provided by the Plant Variety Protection Act in the United States Patent Laws.

PLANT IMPROVEMENT

The applications of biotechnology in improving plants can take many forms. For example, we can produce unique plants that can be protected under the Plant Variety Protection Act. Applications have occurred most rapidly with development of crop plants resistant to various pests including insects and diseases. Applications of biotechnology have allowed us to produce plants that are resistant to diseases or insects in ways never before achievable, and these achievements can be made rapidly to improved cultivars. The most dramatic progress is in controlling plant viruses by incorporating genes into the plant genome that prevent virus infection or multiplication. Biotechnology has also provided new ways to control diseases causes by fungi and bacteria thereby reducing the need for farmers to utilize fungicides and bactericides.

Control of several major insect pests of corn, cotton, tomato, and potato has been achieved by production of transgenic plants containing a portion of the bacterial genome for production of Bt (Bacillus thuringiensis) toxin. Several companies have demonstrated the use of natural plant endophytes that are modified with Bt or other genomes to protect crops from insect pests. In addition, biotechnology is being used to produce complex "natural" biopesticides or pheromone-based products so, useful in IPM programs. All of these new products should reduce the need for synthetic chemical pesticides in crop production.

Another area of plant improvement is the incorporation of herbicide resistance. The incorporation of herbicide resistance has been highly controversial; however, the use of relatively non-toxic herbicides that provide general control of all weeds except the crop containing resistance of tolerance genes, is particularly attractive as we have fewer pesticides to use in our crop protection. This could have significant implication on the need for farm labor.

Biotechnology techniques can be used to select plants which are more efficient in fertilizer and water use. Additionally, we may be able to select plants that are more efficient in their photosynthesis and, thereby, produce more food from the available sunlight. These techniques can also improve environmental tolerance including resistance or tolerance to drought, cold, salt, or toxins.

A very important new area of plant improvement is improving the marketing processing or feed characteristics including unique changes in starches, proteins, fatty acids, or texture. These improvements will allow marketing of fruits and vegetables with improved consumer desirability. An example is the FlavrSavr (trademark) tomato developed by Calgene. This tomato will maintain its firm texture even after it is fully ripe since it is deficient in the polygalacturonase gene—the major gene involved in tissue softening in ripe tomatoes. Similar concepts are being developed for several fruits and vegetables where improved quality and shelf life are important qualities.

Perhaps the most important improvements are in improving the nutritional qualities, and starch, protein, or oil (fatty acids) characteristics. Nutritional quality improvement by increasing or changing amino acid content, increasing unsaturated oil content is being worked on for major crops by several companies. Increased solid content of potatoes and tomatoes improves their processing efficiency. The ability to process certain types of starches and proteins affords the opportunity to produce new food products.

A related plant improvement is the use of plants as bioreactors to produce unique biochemicals such as enzymes, biopesticides, plastic precursors, unique starches and proteins, oils with unique fatty oil composition, or even pharmaceuticals. This concept has been termed "pharming". These products can be used in food or agricultural product processing or as renewable resources in non-food areas. In some situations, these products may replace non-renewable petrochemicals.

Biotechnoiogy has also provided mechanisms to improve plant nutrient utilization and plant metabolic characteristics such as photosynthesis, carbohydrate partitioning, protein and oil synthesis, or nitrogen utilization. These factors could result in lower levels of input by producers without reducing output.

Other applications of biotechnology in plant science includes tissue culture, micropropagation techniques, as well as the development of highly specific diagnostic tests. Tissue culture and micropropagation are of great importance for vegetatively propagated fruits and vegetables or in genetic improvement of long life cycle plants such as forest or fruit trees. Plant cell culture techniques also allow for the development of factory farms where cell cultures would be used to produce foods, industrial or health care products. The use of unique protein or nucleic acid based diagnostic tests play an even greater role in certification programs and are of great importance to regulatory phytosanitary programs in domestic and international commerce.

ANIMAL IMPROVEMENT

Applications of biotechnology and improvement of animal production is particularly exciting. The understanding of basic physiological processes and the endocrinology involved is allowing us to improve the efficiency and productivity of numerous animal species. Bovine Somatotropin (BST) has been developed by Monsanto and approved for improved milk production. A similar hormone, Porcine Somatotropin can be used to produce leaner pork with lower feed inputs. The opportunity to produce lean meat through biotechnology techniques will likely be realized in the near future. Other opportunities include improved feed efficiency, and perhaps even combinations of improved plant types with these improved animal types to produce better food products from animals. Other opportunities include growth promotion and growth regulation through the use of biotechnology-produced enzymes or hormones.

Biotechnology has had its greatest direct impact on animal breeding and genetic improvement. Established technologies such as artificial insemination and embryo transplantation, have been impacted by biotechnology. For example, both embryos and sperm can be sexed and embryos can be frozen or manipulated to produce identical twins, triplets, or even quadruplets. These technologies allow rapid increases in animals with superior genetics, selection of males or females, and the development of genetically identical offspring for research in animal nutrition and physiology.

Animal health has been a major focus for the biotechnology industry. Successful products such as vaccines for diseases such as scours, rinderpest, foot and mouth disease, pseudorabies, blue tongue, and transmissible gastroenteritis have been developed. Diagnostics have been developed for a wide range of diseases. Such rapid and accurate diagnostics are used in animal therapy and are critically important to regulatory quarantines and other issues in commerce.

Several molecular biology-based techniques are available to develop disease resistant animals, leaner pigs and cattle, wool that is easier to wash, and to utilize the "pharming" concepts with animals. Animals are now being used as bioreactors to produce lactoferin for infant formula, protein C for blood clotting, CFTR protein for cystic fibrosis, t-PA for heart attack therapy, hemoglobin for use in blood substitutes, and interleukin 2 for cancer therapy. The use of animals' as bioreactors to produce enzymes, antibodies, hormones, vaccines, or complex molecules, such as hemoglobin make five or ten dairy cows more valuable than 1,000 dairy cows are today.

BIOPROCESSING

Bioprocessing is not new. Man has used microorganisms to ferment raw agricultural products into new foods such as cheese, beer, wine, tofu, etc, for centuries. Recent advances in molecular biology make it possible to extend bioprocessing beyond fermentation. For example with the development of custom design raw agricultural commodities with unique starch, oil, protein, or biochemical content, there are many opportunities to process these products for both food and non-food uses. Renewable resource plant products can be used to replace petrochemicals or other materials in short supply, such as wood. Additionally, bioprocessing can convert waste products or indigestible cellulosic plant materials into food sources for man and livestock or into substrates for microbial fermentation.

Genetically improved organisms are now being used directly in fermentation or as bioreactors to produce acidulants, flavors, flavor enhancers, colors, stabilizers, thickeners, nutrient additives, enzymes, and pharmaceuticals. A particularly exciting area is the use of probiotics. Probiotics are organisms that attach to the intestinal tract and produce compounds that protect us from microbial food contaminants, improve nutrition release in-situ compounds that protect us from diseases or parasites.

Biotechnology has also been used to produce highly sensitive, rapid tests for microbial contamination or microbial toxins in food products. These DNA probes or monoclonal antibody tests will do much to address many food safety problems. Additionally, genetically improved microbes are now used as biosensors for unique products in food processing. For example, microbes can be used to quickly quantify and differentiate specific sugars, alcohols, amino acids, antibiotics, or pesticide residues at very low cost with minimum technical equipment.

SUMMARY

Biotechnology will have significant impacts in our lifetime in agriculture, and will influence our basic plant production, both of crop plants and ornamentals; it will improve the efficiency of our animal production, as well as providing products that are more healthful and more nutritious. Applications of biotechnology in food processing will likely revolutionize this industry. Agriculture is impacted greatly by the public's perception that synthetic food additives and pesticides are undesirable. Biotechnology allows us to utilize naturally-occurring organisms and their products to replace these synthetic products that the public perceives as dangerous. It is, however, important to understand that biotechnology is a new technology, and as such, is not totally socially accepted at this time. The acceptance of food products developed through biotechnology techniques will occur relatively slowly, and only as fast as the public perceives that they are indeed safe.

The exploitation of biotechnology in agriculture is likely to be a very diverse business, not dominated by any one or very few companies. This is because these techniques provide tremendous flexibility, and can be exploited with relatively small capital inputs. This is particularly true as we see the regulatory arena becoming more organized. Entrepreneurs have particularly fertile ground in the land grand university systems. Scientists there are developing unique ideas and potentially new products that can be patented and offer significant business opportunities.

It is critical that the research base be maintained if the United States is to retain its competitive advantage in biotechnology. The federal government has shown significant leadership by funding basic research in this area, in particular genome mapping of both plants and animals. It is also critical to maintain the educational institutions such as the land-grant universities that will train people for employment in jobs where biotechnology is important. We are now where the computer industry was with the first silicon chips. Following this technological breakthrough, there was, and continues to be a high demand for electrical engineers. Today there is a demand of personnel well trained in the technology of biotechnology.

It is estimated today that agricultural biotechnology accounts for more than 9 percent of the biotech market. However, this sector of the biotech market has grown by 48 percent since 1992 and prospects for even more growth are excellent, given a predictable regulatory environment and public acceptance.

Senator ROCKEFELLER. Senator Burns.

Senator BURNS. Thank you, Mr. Chairman. And I appreciate your consideration for catching airplanes here.

And Dr. Jacobsen, welcome to this committee.

As we know, you are pretty familiar with the activities that are going on in Montana State University. And I am very proud of the record there. You rank among the top universities in the Nation in attracting grants for your research center there in your school of agriculture and your biotechnology.

Also, your knowledge of what is going on at Sidney, MT, that I just mentioned a little while ago, and also what is going on even in Butte, MT, when we start dealing biochemically with mine waste, of which we have a problem in the State of Montana. Also, in fact, Montana is the site of the world's largest superfund site, I think. It runs for hundreds of miles.

In an environment where you said awhile ago in your statement—and I am particularly interested in this—where the rules keep changing, give me an example if you can.

Dr. JACOBSEN. Well, for example, if we are developing a new biocontrol microorganism, in many cases, if it is genetically modified, we want to put a marker system in there to monitor where

it goes. Well, we may use that same piece of genetic material in organism A, B, C, D. Under Government rules, we have to go through all of the testing for each organism, even though we have used that same piece of genetic material for our marking system.

That adds a tremendous burden to our research. It slows it down. It would be very helpful if they would say, "If you are using this marking system and you can show that is what you put in that organism, we will allow that to be used in your field trials for marking," rather than going through maybe 1 or 2 years of efforts before we can go to the field with our research.

Senator BURNS. The biotechnology research in the northern plains out in Sidney, MT—and I brought up the deal with controlling the weeds up in Judith, as you are probably familiar with up there in that part of the Lewis & Clark National Forest—are we making progress on that?

Dr. JACOBSEN. At this point, through the release of insects that have been imported from other parts of the world to control leafy spurge and knapweed. These weeds have rendered really useless about 6 million acres in the West, both to wildlife and to livestock grazing. Some of these insects are doing a pretty good job. I think we are getting a handle on leafy spurge.

Now, you mentioned the Sidney Research Station, and we have a lot of that research at Bozeman. You might say, "Well, why cannot you do it one place or the other?" The weak link in biological control is you have to do it to fit the environment that you are working in. We will never have a biological control that works in all environments, such as we might see with a pesticide. It is going to be rather environment- or site-specific. And that is why you need to work in the different environments.

Senator BURNS. Those are the two main questions, I think, I have for Dr. Jacobsen. But I appreciate the work that they do in those controls and the work they do at Montana State University. And I appreciate what you brought up today.

We will continue, as Senator Rockefeller stated before, on S. 4, I think we are going to find that we are going to have a partnership between the Government and people like yourself and institutions like yourself across this country. Because we know that that partnership has to take place. We know we live in a changing world. And it was through the leadership of Senator Rockefeller that I think we can do that.

So, I appreciate that very much.

Thank you.

Senator ROCKEFELLER. Thank you, Senator Burns.

So that you can catch your plane——

Dr. JACOBSEN. I have got a little bit of time.

Senator ROCKEFELLER. Yes, but it is rush hour, so I am only going to ask you one question. Do you have bags to check?

Dr. JACOBSEN. No. [Laughter.]

Senator ROCKEFELLER. That saves you about 15 minutes.

When you talk to your students, are they studying agriculture, are they studying agriculture biotechnology? What course do you offer?

Dr. JACOBSEN. Biotechnology is really taught in virtually all segments of our agricultural education, whether it be economics or

agronomy or horticulture or animal science. I will tell you, because of our perceived need for trained people, we are now starting a new undergraduate program in biotechnology. Students will take the first 2 years in common. DNA is common to all life. Then in their junior/senior years, they will either specialize in plant biotechnology, animal biotechnology, or microbial biotechnology.

Senator ROCKEFELLER. And will they all go out and get jobs? You know, two-thirds of Americans who graduated from college last year did not get jobs. It is sort of a stunning factor. But do your students, because of the explosive growth—what it is, a 48-percent agricultural biotechnology industry growth since 1992? That is explosive. Do they have confidence that they are going to be getting jobs? And what kinds of jobs do they go into?

Dr. JACOBSEN. Senator Rockefeller, maybe Montana State is an exception.

Senator ROCKEFELLER. It is. Senator Burns tells me that every day.

Dr. JACOBSEN. Eighty percent of the kids that graduate out of the college of agriculture get a job in the field of their choice.

Senator ROCKEFELLER. Eighty percent of them do?

Dr. JACOBSEN. Yes. Most of all them—we do followup surveys—most all of them do get jobs.

The agricultural biotechnology degree is meant to serve as two things—for those that might want to go on to graduate work, whether it be in animal, veterinarian medicine or in the plant side, or microbial microbiology.

The other is to provide people what I call the technical positions that are paying $25,000 to $30,000 a year or slightly more, beginning salaries, that companies need.

One of the interesting things is the business school says we would like to have another year added on with business training. I suspect those people with the business training, plus the technical training, in many cases, could nearly write their own ticket.

Senator ROCKEFELLER. My last question. Just stretch your mind and think about 15 or 20 years from now. What kinds of things do you see happening in agriculture biotechnology? What are some of the possibilities that we might see?

Dr. JACOBSEN. I think the opportunity to do value-added processing, even in rural communities or rural States like Montana, or anywhere, is there. We are going to be producing crops that have very high yields of very high-value compounds, biochemicals, enzymes, perhaps pharmaceuticals. I see that in the future.

I see a future, if we develop it properly, where biocontrol, rather than pesticides, will be the rule. It is certainly within our reach. I do not think we will ever do away with all pesticides, but I think that clearly this is an alternative and something we need to work on.

The opportunity in bioprocessing I think is absolutely incredible. Through microorganisms now or even plant cell culture, we can produce plastic precursors and other compounds that right now we are dependent on nonrenewable resources for.

Agriculture is the renewable resource industry. And I think that it is taking the technological steps to really come to the forefront

in more than just food production. It is going to probably give us a lot of our industrial feedstocks also.

Senator ROCKEFELLER. Are you familiar with Los Banos and the green revolution?

Dr. JACOBSEN. The green revolution; yes.

Senator ROCKEFELLER. In other words, they found in Asia that they could take the rice that they were growing and make it something like eight times more productive on the same amount of land. And many say that that has helped enormously to prevent starvation in China, which does not have that much, and in India.

Earlier you talked about—I am not sure if you said barley or wheat—but you were talking about a relatively small portion of it being used for food and a larger portion being used for other things. But just taking food itself, do you see the United States, and others as we do this, being able to—and this will sound slightly naive—but sort of supply food for the people who do not have it across the world? We will become so efficient that food will be—if we can distribute it, it will be available because the quantities will be so great?

Dr. JACOBSEN. I see two things. The world population is growing very rapidly. I think we are going to be a massive exporter of food to the developed and the developing world everywhere. However, if we can get those people in developing nations well fed, so that they do not worry about where their next meal is coming from and they now have some discretionary income to do other things, they are going to become our customer and buy other things that we make—most likely things that have some added value.

So, food security over the world, biotechnology is going to play a great role in that—not the sole role, but a great role in that.

Developing nation farmers have more problems with buying inputs than American farmers do. It is very expensive. If we can produce crops that are pest-resistant, that is a tremendous opportunity for them that I see as their food security gets greater, as we have seen with China. I believe I saw some statistics that since 1980, personal income in China has gone up fourfold. We all look at China now as one of the great hopes as an export market for the United States. And I think same of that came because of food security.

Senator ROCKEFELLER. All right, Dr. Jacobsen. We are going to let you catch your plane.

Dr. JACOBSEN. Thank you.

Senator ROCKEFELLER. And we all thank you very, very much for coming. It is a long way. Believe me, I found that out a couple of weekends ago. And you have added a great deal.

So, thank you very, very much.

Dr. JACOBSEN. Thank you, Senator Rockefeller.

Senator ROCKEFELLER. We are joined by Senator Kerry, who has an enormous interest in this subject of biotechnology industries. We have yet to hear from Mr. Perez and Mr. Skaletsky, but I would welcome any comments or thoughts that Senator Kerry would have coming into this.

OPENING STATEMENT OF SENATOR KERRY

Senator KERRY. Mr. Chairman, thank you very much.

First of all, thank you for having this hearing. And I apologize for being late, and I apologize ahead of time for having to leave shortly for another meeting. I wanted to come by not just because Lexington, MA, is represented here by Mr. Skaletsky, but this industry is obviously at a critical point in its own development. And the health care bill and some of the thoughts being circulated with respect to pharmaceutical companies and the impact on stock and investment is having an impact on companies in our State and elsewhere in the country and their ability to be able to attract capital and remain competitive.

It is a highly capital intensive industry as you know better than anybody and as testimony has shown. I have taken time to read your testimony, Mr. Skaletsky, and I think it is very thoughtful and helpful to us.

There also ought not to be a confusion between traditional pharmaceutical companies and the biotechnology companies. And I think we need to try, and I know you will and you have been particularly sensitive to this as chairman of this committee, to figure out how to minimize that impact—if there is a way—or at least to maximize the ability of these companies to continue to develop these products which have, I guess, a return of investment lifespan of anywhere from 2 to 3 years or something—very, very short, before others are out in the market. So, it is very hard to recoup unless there is some recognition of that process.

So, I just want to thank you. Your testimony has been very helpful.

Mr. Chairman, I think it is very, very important to be looking at this kind of cutting-edge technology and the jobs and opportunities that it will create for us, not to mention the good that will come out of it.

I have not needed it yet, but I may soon need some of your product for cholesterol or for some aspect of your digestive benefits, and I look forward to learning just how that is going to work as the need arises.

Thank you, Mr. Chairman.

Senator ROCKEFELLER. Thank you, Senator Kerry.

We have actually been discussing a little bit the sensitivity of the pharmaceutical industry to the health security act or the Clinton health bill, and the perception—whether this is a matter of perception or a matter of reality—in that price controls are not in fact involved, but the perception exists even though there is no ability of the Breakthrough Price Commission to impose prices whatsoever. It is just that in Medicare, the Government is such an enormous purchaser of pharmaceuticals—probably about one-half, about 50 percent of all pharmaceuticals in the country.

Whether or not as you are looking at the area of cost containment whether or not the Government has a right to at least express a view, not set any price and participate in none of that as to what the prices might be—and actually, the HHS Secretary is precluded or the Commission is precluded only to looking, I believe, at those drugs which are deemed to be inappropriately or excessively priced.

But it is a very interesting discussion, because is it reality or is it perception? And perception, of course, becomes reality, and that

is a very important point. Because if the pharmaceutical industry believes that without any deviation, then we are kind of stuck. And so we have been actually into that somewhat.

Gentlemen, I do not know who would like to go first. Mr. Perez, you are in the middle of the table, so why do you not do it.

STATEMENT OF J. PETER PEREZ, PRESIDENT AND CHIEF EXECUTIVE OFFICER, ENVIRONMENTAL REMEDIATION, INC.; ACCOMPANIED BY JOHN CHRISTIANSEN, VICE PRESIDENT OF TECHNOLOGY

Mr. PEREZ. Thank you.

I am Peter Perez. I am the president, founder, CEO, and owner of Environmental Remediation, Inc., and the International Biochemicals Group. I did bring with me John Christiansen, who is our vice president of technology, just in case your questions get awfully technically.

We are a company that develops, produces, and utilizes natural microbes to degrade hazardous waste and for different types of environmental concerns and cleanups. I do underline the word "natural" here.

I consider myself an entrepreneur and a businessman. I started this company in 1982. And we have, through bootstrapping ourselves and through acquisition, grown to over 140 employees throughout the world. We have plants in Louisiana, Texas, and in Dublin, Ireland. So, I can comment if you wish a little bit on the European market, since we are into it fairly heavily.

We are a perfect example of the concept emphasized by Vice President Gore of how different types of environmental regulations and laws throughout the world can spur and produce economic growth. And we are living proof here that that does work.

Unlike Ms. Conte, we are a privately held company, and we have maintained 100 percent of our capital in growth on retained earnings, which is very difficult if you have ever tried that. It is kind of an unfounded way to do it in this particular industry, however, we have been able to do this.

Environmental biotechnology is a little different. It is not near as big as the environmental health or biotechnology pharmaceutical industry, but we are a very real industry. We have coined the term "bioremediation." I think you have heard that a couple of times today. And, with your permission, we did bring a videotape.

Senator ROCKEFELLER. Yes, I have been kind of wondering what that was about.

Mr. PEREZ. Since a picture is worth a thousand words—let me tell you that CBS did this on our company about a year ago, and we have in it several sites where they utilize bioremediation and have been very successful in this. And it may interest you.

[Whereupon, a videotape was shown.]

Mr. PEREZ. That gives you a glimpse into an industry that is very young and just beginning to grow. To give you a little bit of an idea on the growth rate, we have some charts here on the left. The first chart is the number of companies, strictly the number of companies between 1984, which was 25 firms in our business, to the present time where there is over 125. So, that is a growth rate

of 500 percent in a 10-year period. As you can see if you extrapolate that on out, we do have a fairly decent growth rate.

The next chart is the amount of revenues that we have in our industry. This shows you from 1994 to the end of this century. As you can see, we do have areas in our growth rate that we are projecting to just keep climbing in revenues. There is one—the green chart is what they call UST market, which is the underground storage tank market, and that particular market will start decreasing in this century because that market is being cleaned up.

And the final thing is we do have a number of new technologies that we are utilizing in the environmental biotechnology business. This is one of the new ones. Let me just say something. One of them is—one of the newest technologies is what we call MEOR, microbial enhanced oil recovery.

Another one is this—is bioslurry injection. What this does is take mixtures of bacteria, nutrients, and a time-release form of oxygen. We have a mechanism to inject it into the ground to where this—the slurry does a job in degrading the organics in a particular—in an impacted area under the ground. We do not have to move this material over the road. We do not have any incinerators. It is very innocuous and a nondangerous way to take care of contamination, especially in areas that you do not want to disturb the ground.

So, as you can see—now, this is not a widely used technology here. Most of the widely used technologies are what you saw in the picture, which is a form of land farming and what we call liquid solids reactor, contact reactor technology.

So, in closing, what our part of this industry needs—and we are a very humble and we are a very simple part of the industry, after listening to some of the testimony today. But what our part of this industry needs is, first, your support in the biotechnology industry as a whole. Next is a mechanism to teach, to teach the leaders, the leaders of our country, what we are doing, so that they will be able to support us in the future.

We need support in the renewal of the Clean Water Act and reauthorization of the superfund, especially reauthorization of the superfund that includes permanent solutions to our environmental problems; not temporary or containment-type solutions, but permanent solutions to our environmental problems.

And the final thing we are looking for as businesses is to basically not tax us to death. If you are familiar with the new rules regarding sub-S corporations, and most companies are sub-S, subchapter S corporations, it really does increase our taxes quite a bit. In fact, most people are amazed to know that our taxes are about 46 percent of our net earnings. Now, that 46 percent of our net earnings means that that is less money that we have to go into growth, go into hiring new people, go into research and development, and we do spend quite a bit of our net earnings on research and development.

And thank you very much. That is our testimony.

[The prepared statement of Mr. Perez follows:]

PREPARED STATEMENT OF J. PETER PEREZ

I am J. Peter Perez, President and CEO of International Biochemicals Group (IBG), a company that directly employs over 140 people in the United States and

Europe. Our business is to perform environmental services and to manufacture and market microbial based products that are used to biologically degrade organic waste.

AN ENTREPRENEUR'S STORY

Let me first tell you about my company. The formation of the companies that resulted ultimately in IBG is a real life Horatio Alger "Rags to Riches" story. In 1982, I founded a small company that blended and distributed microbial products that are used to biologically treat organic wastes in the pulp and paper industry. Biotreatment is an all encompassing term covering the use of bacteria in biological treatment of any form of unwanted waste, whether in an industrial waste water plant, municipal waste water plant, fast food restaurant grease trap, home septic system, or hazardous waste site. In 1984, we expanded to include what is now referred to as bioremediation, a form of biotreatment that uses bacteria to breakdown unwanted pollutants in soil, sludge, water or air into carbon dioxide, water and innocuous salts. Although there was a lot of interest in this developing technology, initially there were very few companies willing to take a risk to invest in the new technology.

Later, during the 80's, environmental concerns moved from fringe groups to center stage. Major environmental disasters began to play a significant roll in changing both the law and consumer habits. Although we were a privately held, undercapitalized firm, we were able to take advantage of the "green movement" and use retained earnings to grow into the world's leader in the manufacture and sale of commercial microorganisms that are used for biotreatment. We are an illustration of a concept emphasized by Vice President Gore, that environmental regulation can provide an incentive for economic growth. Government pollution control requirements create the demand for most of our products.

Over the years IBG has been recognized locally and nationally on a number of occasions for both its business and technical successes. Such recognition includes a national Small Business Administration (SBA) Minority Business Award (1989), Louisiana SBA Business Award (1989), a prestigious Inc. Magazine Top 500 Private Company Growth Award (1991), and numerous trade and local awards. We have also been featured on CBS This Morning and in Science & Technology, Forbes, and Nations Business. I give full credit to the men and women who persistently and untiringly committed themselves to making our American technology the best in the world.

IBG's mission is founded on the basis of customer satisfaction, product value, progressive research and development. We now have plants in Baton Rouge, Louisiana; Houston, Texas; and Dublin, Ireland. With major research facilities in both Dublin and Baton Rouge, IBG is in the world's best position to advance environmental microbial technology into the European Union, Eastern Block, Middle East and Pacific Rim. We are implementing a major expansion at our Houston facility to supply increased demands in the United States, Canada, Mexico and South America. Not only does the future look bright for IBG, the future is bright for the entire environmental biotreatment industry.

The key to sustained economic growth and advancement of our industry is research and development. R&D is extremely important to our firm and to every other company that is in the environmental biotechnology business. Our company and most others in our industry are investing large percentages of both capital and earnings to research new methods of biotreatment, to develop new products, and to study their application to solve real world problems. We need to work hand in hand with our government to transfer proprietary technology from the government sector to the private sector so that we can continue to lead the world in this field. Our industry works closely with most universities to assist in academic transfers. We believe our government should continue to sponsor and promote such programs as R&D tax credits, small business innovative research grants, advanced technology programs, cooperative research and development agreements, or any other type of sensible programs that have our U.S. government and private sector working on the same team.

HISTORY OF OUR TECHNOLOGY

Many people believe that bioremediation and biotreatment are new and unique. Actually, although we are a very specialized technology, microbial technology was developed in the late 1940's in Roanoke, Virginia. In the early 1950's, during the Korean conflict, Dr. Howard Worne was commissioned by the U.S. government to research and develop a solution to keep army combat uniforms from biologically degrading in the moist, humid, middle Asian climates. Dr. Worne isolated a microorganism that very rapidly degraded fabrics that were heretofore thought to be non-bio-

degradable. His curiosity and vision led Dr. Worne to the conclusion that if microorganisms could degrade "non-degradable fabric", they could also degrade other materials that were previously thought to be non-biodegradable. Dr. Worne's next quest was to isolate an organism that would degrade phenol, which was a recognized organic pollutant at that time. What we have in the bioremediation industry is a classic example of a commercial spin off of government research and development. From Dr. Worne's humble beginnings an entire industry was born.

From Dr. Worne's original discoveries and innovative thinking came our bioremediation industry. The industry now is able to degrade most organic contaminants including some recognized pollutants such as creosote, pentachlorophenol, and some forms of poly-chlorinated biphenyl (PCB's). Some examples of aggressive biotreatment are the following:

- In 1989 Amoco Oil Company began using biotreatment to efficiently, economically, and safely degrade refinery oil and waste at a Sugar Creek, Missouri site, just a few miles from the birthplace of Harry Truman.
- Several companies, including ours, successfully tested products to degrade oil spilled from Exxon Valdez in Alaska under the excellent guidance and supervision of the U.S. E.P.A., NETAC, and the Coast Guard.
- Specialty bacteria are tested and used to remove Sulfur from high-Sulfur coal to make this product safe for use in our environment.

Bioremediation has come a long way since the 1940's, and we are now poised on the threshold of a new era ready to use microorganisms to solve environmental problems.

The mid-80's found an explosion in small, entrepreneurial firms that wanted to get into the biotreatment field. Most of the companies formed during this period of time have gone through the same type of growth pains as ours (see chart printed at conclusion of testimony). Several companies have utilized biostimulation, the simplest form of bioremediation, to treat the hydrocarbons leaking from underground storage tanks. Biostimulation is the method that utilizes nutrients and oxygen sources (such as peroxide) to stimulate the microorganisms that are naturally found in the soil. These naturally occurring microorganisms utilize unwanted hydrocarbons as a food source to clean the soil. The biostimulation market has been very good over the past few years but is extremely finite. It is believed that this market will decline rapidly over the last half of this decade.

Biodestruction of the more complex organics is the market of the future. Effective and efficient degradation of these complex organics requires laboratory stressed, naturally occurring microorganisms or, in some cases, genetically engineered microorganisms. In the present growth stage of our industry, microorganisms are stress-acclimated in the laboratory. This process is extremely cost effective and efficient, but it does have its limitations.

When natural organisms reach their degradative limits, genetically engineered microbes (GEM's) are an alternative. GEM's are microorganisms that have been genetically modified in such a way that they not only survive but thrive on substances found in a highly toxic environment. Rightfully so, the Environmental Protection Agency and other government agencies have been cautious in allowing the unregulated use of GEM's. Although use of GEM's is relatively uncommon in today's bioremediation industry, we believe that GEM's will become more commonplace in the next century. We also believe that there will be a number of additional regulations and controls placed on the release of this type of microorganism. Our industry is concerned that the government will imposed burdensome regulations on GEM's and stifle this emerging technology. We may return to this Subcommittee and ask for help if the regulations overreach and impose excessive burdens.

In the future bioremediation techniques and biological products will address new customer needs. This will include:

- Cleaners that use bacteria and enzymes to take the place of caustic, acids, and toxic solvents.
- Products which increase the yield of petroleum in "stripper" wells which there are more than 20,000 in the U.S.
- Products to manage and increase agricultural yield and control and minimize plant disease outbreaks
- Tracers to determine flow outlets and retention time
- Laboratory aids
- Paper machine slime control
- Algae control in decorative ponds
- Agents to increase yields in aquaculture

Some products are several years away from commercialization while others are nearly ready for sale. We anticipate that in 20-30 years biologically produced chemicals will replace toxic or caustic chemicals in hundreds of applications.

SAFETY AND EFFICACY

The present day technology that uses mainly biostimulation and/or commercial microorganisms is extremely safe and effective.

Consider this example. A farmer. while plowing a field, cracks his tractor's crank case. The crank case oil leaks out onto the soil. There is now a small, contaminated waste site. Let's assume that this site is not immediately disturbed. While some of the lighter end hydrocarbons evaporate, most of the hydrocarbons will soak into the soil and bind themselves in the soil matrix. Then an amazing thing starts to happen. Nature takes over and tries to clean up this problem. Naturally occurring bacteria on the outer rings of the contamination site acclimate themselves to utilize the hydrocarbons as a food source. As these bacteria devour the hydrocarbons, they grow and proliferate many times. Ultimately, the natural soil bacteria will consume all of the organic contamination that occurred from the spill as a food source. Once these bacteria have finished degrading the organics, the number of bacteria will revert to the natural level of bacteria that proliferated in the soil before the spill.

Let's take this scenario one step further. Several weeks after the spill an energetic microbiologist goes out to the site and carefully isolates some of the bacteria that have been degrading the organics found in the soil. He takes the specialized bacteria back to a laboratory where he reproduces this super bacteria so that it can be targeted to degrade other similar forms of hydrocarbons. Then the bacteria is grown into extremely large quantities and placed in a medium that can be dried and stabilized. The result is a commercial microbial culture that can be sold all over the world to solve similar problems. A new market has emerged!

The preceding example sounds very simple. However, the process can be very complex. U.S. scientists from universities, government, and private companies have taken the lead in developing stress-acclimated microorganisms for use all over the world in the biotreatment market. Commercial microbes are used in the bioremediation, industrial waste water, municipal waste water and commercial microbial markets. For instance, microbial blends have been developed to replace the caustic compounds presently used to open clogged drains in your home. Also, for the past 30 years microbes have been sold under the name "Rid-X" into the consumer market to improve the function of septic tanks.

In the mid-80's, the industry received some opposition from the public with regard to our using bacteria to clean up hazardous and non-hazardous waste sites. However, after numerous public meetings, the public was reassured that the natural bacteria were safe and harmless and that the bioremediation methods utilized were much less offensive than incineration or land burial. Presently, biotreatment methods are advocated by most environmental groups and receive little, if any, opposition.

U.S. COMPETITIVENESS

The United States has a tremendous lead in the biotreatment market. As shown on graph 2 (attached to the end of this testimony) our industry will achieve excellent growth between now and the end of this century. The underground storage tank (UST) market will decline after 1996 as these sites are being cleaned up. However, other forms of biotreatment will become available to replace these lost revenues.

Our company, for instance, presently sells into over 40 different countries throughout the world. We are a net exporter of products that are produced in the United States. Uke ourselves, our main competition also sells a significant percentage of its product outside of the U.S. I firmly believe that it is the innovation and high productivity of the American worker that has made us so competitive in the market. For instance, our products are used extensively throughout Germany, Italy, France, and England. Although we do supply some of these markets out of our Irish manufacturing plant a significant percentage of the products come from the United States.

Unless U.S. businesses lead research and development efforts in environmental microbial science it will not be long before both European and Far Eastern countries start to replicate our successes and erode our market edge. Other progressive countries in bioremediation and biotreatment are Germany, Luxembourg, Italy, Korea and Taiwan. Not far behind these countries are Japan and Australia. We are on the threshold of a new era in ecological treatment of mankind's pollutants. The bioremediation industry can lead our country across the threshold into a new realm of world trade if our United States government does not stifle our efforts. The business leaders of the U.S. biotreatment industry need the support of the United States government to maintain our edge over foreign competition and to continue to make

the United States a net exporter of microbial products and bioremediation services in order to do our share to balance trade.

POLICY NEEDS FOR THE BIOTREATMENT INDUSTRY

At this point in our growth, the biotreatment industry's needs from this Subcommittee are not complex. We need support of our technology, the freedom to run a business, and restraints from over regulation in order to be number one in this industry and widen the gap between us and foreign competition.

First, we ask this Subcommittee and the leaders in the U.S. government to support U.S. E.P.A. Administrator Carol Browner in her efforts on behalf of the bioremediation/biotreatment industry. Our industry was relatively unknown until the previous E.P.A. Administrator William Riley learned about our technology and dubbed himself the "flag waver" for our industry. This flag was graciously passed on to Administrator Browner who has strongly supported us in every way. We ask that the U.S. government continue to set up teams of scientists to learn more about environmental biotechnology and to pass wisdom down to local regulators.

Second, knowledge and education are the keys to achieving our goal. Subcommittee hearings such as this are an excellent beginning. However our industry leaders must work with the leaders of our government to expand this knowledge and spread our wealth of information. Specifically we ask that the Subcommittee hold a hearing on the impact of government regulations in encouraging commercial ventures such as ours.

Third, we ask that this Subcommittee help to organize a roundtable or conference to bring together government policy makers and scientists, private sector manufacturers of biotreatment technology, consumers of our technology, and environmental and other public interest groups. It could be hosted by the Department of Commerce and/or the Environmental Protection Agency. One outcome of such an event would be to set a government strategy for helping our industry compete in international markets and ensure that the government does not unintentionally damage our ability to compete. We would be happy to help organize such an event. Our organization volunteers to help organize this momentous event.

Fourth, Congress and this administration can assist the growth of our biotreatment/bioremediation industry in several ways:

1. Support the reauthorization of the Clean Water Act, while allowing industry to make their own choices for the type of process employed.

2. Support the reauthorization of the Superfund Legislation but alter the program to:

- Limit the application of joint and several liability to force early clean-up actions
- Proceed with the clean-up action independently of cost resolution. This can be done by having EPA take sites where no clean-up action has taken place and specify the remedy and assign clean-up contractors. The cost would be allocated by EPA on any PRP's which have not yet sampled.

3. Allowing broad patenting and protection methods for living organisms, bacteria, since in bioremediation applications, said bacteria acts as a miniature chemical manufacturing process.

Fifth, we ask the Subcommittee to support our efforts in starting and maintaining competitive businesses in the United States. Every day the world of international trade becomes more competitive. Our competitors are starting to spring up in every corner of the world. The bioremediation/biotreatment industry just like other major industries in the United States must compete with companies which receive tremendous government assistance such as Japan, Taiwan, China and the European Union. Our industry works hard to protect itself from theft of our products and intellectual property. Patents alone are not the answer. Cooperative agreements between governments to set up arbitration committees to assist in disputes between business from different countries would make a lasting impact on maintaining a competitive edge in the world market.

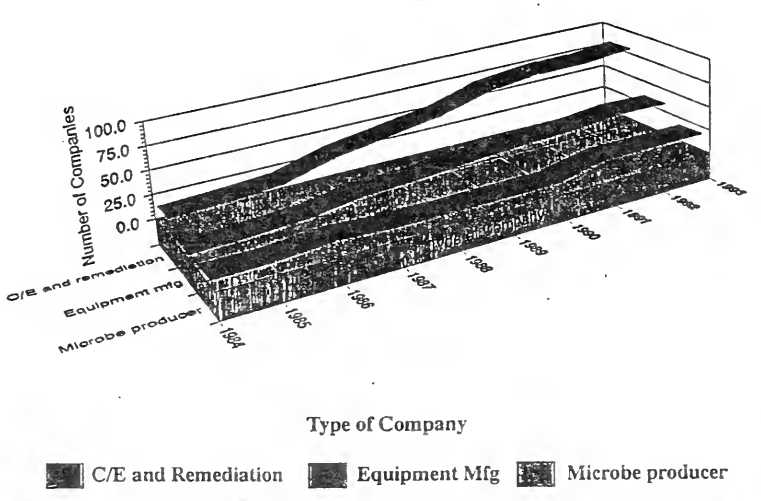
Sixth, we ask you to support new business in the United States of America. First, capital formation, whether through public or private sources, must be made easier. Today, it is hard to start and operate a business in the United States. Regulation of capital formation, the progressive tax structure that has been imposed upon business throughout the years, the fear of future regulation, operating costs, and tax burdens oppress U.S. businesses.

Finally, we ask that the Subcommittee use its influence and prestige to assist U.S. businesses in alleviating the problems of ever increasing tax burdens. As in all other industries in the United States, in our industry profits are invested for research and development, equipment, and people. Most of the companies in the biotreatment industry are small, entrepreneurial firms. These firms reinvest earn-

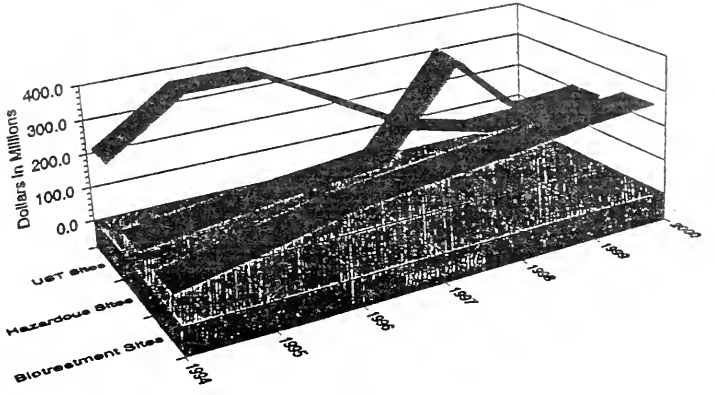
ings for growth. Increased taxation of retained earnings impedes growth and makes it extremely difficult to compete throughout the world.

I appreciate the opportunity to testify and am pleased to answer you questions.

GROWTH OF BIOREMEDIATION/BIOTREATMENT COMPANIES
1984-1993



BIOREMEDIATION/BIOTREATMENT MARKET FORECAST
1994-2000



Senator ROCKEFELLER. Thank you, Mr. Perez. That was interesting and excellent. Mr. Skaletsky.

STATEMENT OF MARK SKALETSKY, PRESIDENT AND CHIEF EXECUTIVE OFFICER, GELTEX PHARMACEUTICALS, INC.

Mr. SKALETSKY. Thank you, Mr. Chairman.

I am sorry Senator Kerry had to leave. I wanted to thank him.

Senator ROCKEFELLER. No, that is my mistake, because I should have called on you first, and I apologize.

Mr. SKALETSKY. Oh, that is fine. Many of us in Massachusetts have an opportunity to see Senator Kerry. He has been a real supporter of our industry and will continue to be so, I am sure.

Senator ROCKEFELLER. Well, I am seeing him later in the day and I will tell him you said that.

Mr. SKALETSKY. Thank you very much. I am a little bit nervous sitting next to a company that has retained earnings. I am not sure I would know what to do with those if I had any. [Laughter.]

My name is Mark Skaletsky and I am CEO of GelTex Pharmaceuticals. GelTex is a Lexington, MA based private biotechnology company founded in 1992 and we currently have 17 employees. We are funded from investments from individuals and venture capitalists.

Our mission is to design, develop, and commercialize new nonabsorbed therapeutic products that act in the gastrointestinal tract. We are developing products for cholesterol lowering, phosphate reduction for patients who suffer from kidney disease, and products to treat several infectious diseases such as group B strep, a bacteria that will result in the death of 2,000 infants yearly while leaving many others mentally and/or physically handicapped.

I have been involved in this industry for 14 years and have helped four companies which are in various stages of development. This is an industry that is very exciting from the standpoint of research and developing innovative treatments for diseases. However, as has been said, the industry is also quite risky from the standpoint of being able to raise enough capital to finance our products and provide a return to our investors.

We have all heard of the enormous costs involved in research and developing and commercializing new therapeutic products. These risks are spread over a 5- to 10-year timeframe starting with the hope that the technology can yield a product candidate through the regulatory approval cycle, and finally, hopefully, market acceptance. Our goal is to develop these innovative products as quickly as possible and see them being used to treat people suffering from disease and/or to prevent disease from spreading.

My family has personally benefited from a product developed by the biotechnology industry. I have a daughter who has Gaucher's disease, a lipid-storage condition that results in severe medical problems, including bone decay. Until recently, this condition was not treatable, with the result being quite debilitating conditions for the patients. A miraculous treatment, Ceredase, is now available for this disease, a result of a biotechnology company working with the NIH to develop this product.

No large pharmaceutical company was interested in developing this product because the market was not large enough. Were it not for the biotechnology company willing to invest in the product, I would hate to think what my daughter and others like her would be suffering through today. And this is what we are all about, de-

veloping products through innovative technologies to treat people. We must be careful not to get too caught up in the economic arguments of drug development and forget the people who we are trying to help.

Not only is this industry an important contributor to the health of the U.S. economy, but it also has been cited as one of several critical technologies that will drive U.S. productivity, economic growth, and competitiveness over the next century. Our competitive edge is due to the combination of our technology base and our capital base. Europe and Japan continue to develop technology, but lag behind in their ability to develop and commercialize technology because of their lack of venture capital and public equity markets.

As an industry, as you heard, we support health care reform, including universal coverage, cost control, and basic research funding. During this debate and eventual legislation, we must keep in mind that health care reform will only work if it spurs innovation. Many industries have shown that the only way to lower costs substantially is through innovation; health care is no exception.

America should rely on the biotechnology industry to improve the quality of our health care system and contain costs. We need a national bias in favor of medical innovation, and we look forward to working with you and the committee on this issue.

Thank you.

[The prepared statement of Mr. Skaletsky follows:]

PREPARED STATEMENT OF MARK SKALETSKY

Good afternoon. My name is Mark Skaletsky and I am the CEO of GelTex Pharmaceuticals. GelTex Pharmaceuticals is a private biotechnology company founded in 1992 which currently employs 16 people. We are funded with investments from individuals and venture capitalists. Our mission is to design, develop and commercialize new, non-absorbed therapeutic products that act in the gastrointestinal tract, for the selective elimination of substances that either result from certain disease states or the reduction of which will have a beneficial medical effect. We are developing products for cholesterol lowering, phosphate removal for use with patients who suffer from renal disease, and to treat several infectious dises such as Group B strep, a bacteria that will result in the death of 2000 infants yearly, while leaving many others mentally and/or physically handicapped.

You have heard an overview of the competitiveness of the U.S. biotechnology industry and our policy agenda here in Washington. Let me focus specifically on the biopharmaceutical sector of the biotechnology industry.

BACKGROUND ON BIOPHARMACEUTICAL INDUSTRY

Let me begin by mentioning some of the milestones in the genetic revolution. In 1961, a technique for recombining genes was patented, setting the stage for the biotechnology industry. In 1975, Genentech, the first biotechnology company, was founded in South San Francisco and the first cancer-causing gene was identified. In 1983, the gene for human insulin was cloned. The first genetic marker for cystic fibrosis was found in 1985. In March of 1993, the gene behind Lou Gehrig's disease was discovered. These are only a few of the remarkable achievements the biotechnology industry has already provided.

There are currently 23 biotechnology therapeutics/vaccines approved for sale by the Food and Drug Administration (FDA). The first of these was approved in 1985, and the latest was approved in February of this year. The biotech medicines currently available for purchase treat a variety of indications: AIDS, diabetes, dwarfism, hepatitis, heart attacks, anemia, leukemia, renal cancer, organ transplant rejection, Cystic Fibrosis, Multiple Sclerosis, and Kaposi's sarcoma. Drugs and vaccines that are now being developed by emerging biotechnology companies will treat such intractable diseases as cancer, arthritis, Alzheimer's, heart disease, osteoporosis, and genetic disorders. Other biotech companies are researching therapies for burns and blindness.

The risks for companies developing biopharmaceutical products on the way to the market are enormous. In fact, it is estimated that only five in 4,000 compounds screened in preclinical testing make it to human testing. One of those five tested in people is approved for sale. The approval process is approximately seven years for a biopharmaceutical, according to a recent article in BioPharm. The same article added, "The seven-year development time for biopharmaceuticals is an average for the first successful products derived through biotechnology. This figure does not include all biopharmaceuticals that reached the stage of clinical testing during the 1980s. Because the biotechnology industry is still young, products with relatively long development times are less likely to have been approved than products with relatively short ones."[1]

The long odds against a product making it past the scientific risks and the regulatory process make it difficult for companies in the biotechnology industry to convince investors that their company is worth investing in. Investing in the biotechnology industry is risky. That is why it is important to demonstrate to investors that potential rewards are commensurate with the risks.

Without patient investment from venture capitalists, public investors and others, this industry would not exist. The U.S. biotechnology industry dominates international markets because of the convergence of outstanding basic science and sophisticated capital markets.

COST OF DEVELOPING A DRUG

The Office of Technology Assessment finds that the average cost per new chemical entity (NCE) is $359 million.[2] This survey did not cover the cost of developing a biotechnology drug, but analyses done by our industry find that the cost of developing a biotechnology drug may be similar. We know that Genzyme and Amgen, two of our member companies, raised $328 and $264 million, respectively, in equity before they brought their first products to market. In addition, Genentech has spent $1.6 billion on R & D and has four basic products on the market.

Lisa Conte mentioned the incredible research costs of biotechnology companies. We are the most research intensive industry in the history of civilian manufacturing, investing $60,000 per employee in research. The biotechnology industry spends more on research and development, based on R & D as a percentage of revenues and on a per employee basis, than any other industry. The research is expensive for one simple reason; we are advancing basic and applied science at the same time.

FINANCING OF RESEARCH AND DEVELOPMENT

The biotechnology industry is dependent on the equity capital markets to fund its research and development. Very few biotech firms are profitable or can fund their activities from sales of existing products. Banks generally will not lend money to a biotech firm. The overwhelming bulk of our capital comes from the sale and placement of stock.

Biotechnology companies were able to raise a total of $2.8 billion in the capital markets in 1993, compared with $2.5 billion in 1992. However, if you look closer at these figures, you will understand why only segments of the market were open and that the cost of capital increased. A significant portion of the money that was raised last year was in the form of private placements. Taken together, venture capital firms, institutions and even individuals came up with a All 40 percent of all monies flowing to biotech in 1993.[3] Venture capital and private placements are usually seed money that allow companies to begin their reseasch. When a venture capitalist invests in a company, he/she is investing in the science of biotechnology. As a company gets close to commercialization of a product, it usually must "go public" to raise funds from shares traded on the NASDAQ, NYSE or AMEX stock exchanges. Public investors are investing based on their belief that an individual company will be successful. The public stock market is the only place that they can go to raise the enormous amounts of money that are needed to commercialize a product.

Public financing was especially difficult for biotechnology companies in 1993. The American Stock Exchange Biotechnology Index lost 32.6 percent last year. These difficulties are finder displayed by figures comparing this year to last year in terms

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[1] Brigitta Bionz-Tadmor and Jeffrey S. Brown, "Biopharmaceuticals and Conventional Drugs: Comparing Development Time," 44–49, BioPharm, (March 1994).

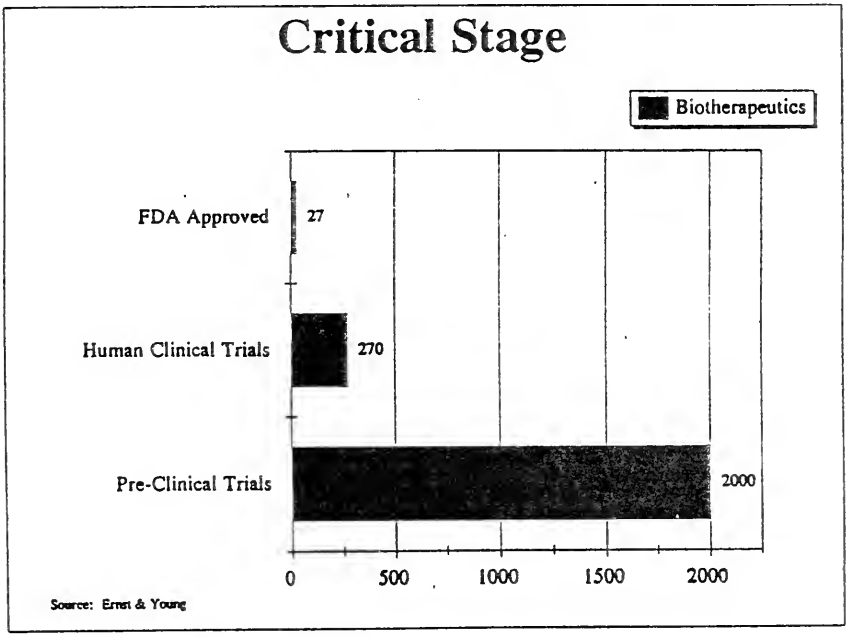
[2] U.S. Congress, Office of Technology Assessment, Pharmaceutical R&D: Costs, Risks and Rewards, OTA-H-522 (Washington, DC: U.S. Government Printing Office, February 1993).

[3] Van Brunt, Jennifer, "1993 Tops Out at $2.9 Billion—and It's Still Coming," BioWorld Financial Watch, 1 (January 10, 1994).

of total public offerings and initial public offerings (IPOs). The average deal size of public offerings in 1993 was down to $23 million, from $28.2 million in 1992. IPOs were down to $22 million in 1993, compared with $26 million in 1992.[4] Several public biotech companies were forced to do Private Investment in Public Equity (PIPE) financings, deals where public companies sell stock to private investors at a discount to their current stock price. According to many press accounts, mezzanine investors were scared by the de facto price controls in the Administration's health care plan because they feared that some widely discussed points of health care reform would mean that they would not recoup their investment in a company that was close to bringing a product to market.

The biotech industry is in a critical stage of development and research (please see chart below). There are 23 biotech medicines that have been approved for sale in the U.S. by the Food and Drug Administration (FDA). Two hundred and seventy biotech therapeutics and cures are now in human clinical trials. According to Ernst and Young, two thousand potential therapies and cures are in early development stages.[5] Now is the time when the biotech industry needs increasing amounts of capital to bring these products to market where they can improve our quality of life.

According to a recent report by Dr. Robert Goldberg of the Gordon Public Policy Center at Brandeis University, fully 75 percent of biotechnology companies have 2 or less years of capital left. Ernst & Young reports that biotech companies are raising capital now at 25 percent of their burn rate (the rate at which capital is being expended.) As has already been mentioned, there are approximately 1,300 U.S. biotechnology companies. That means that a staggering 973 companies will need to go to the market in the next two years or face going out of business, merging or selling rights to a larger firm.



INTERNATIONAL PRICING FOR BIOTECHNOLOGY MEDICINES

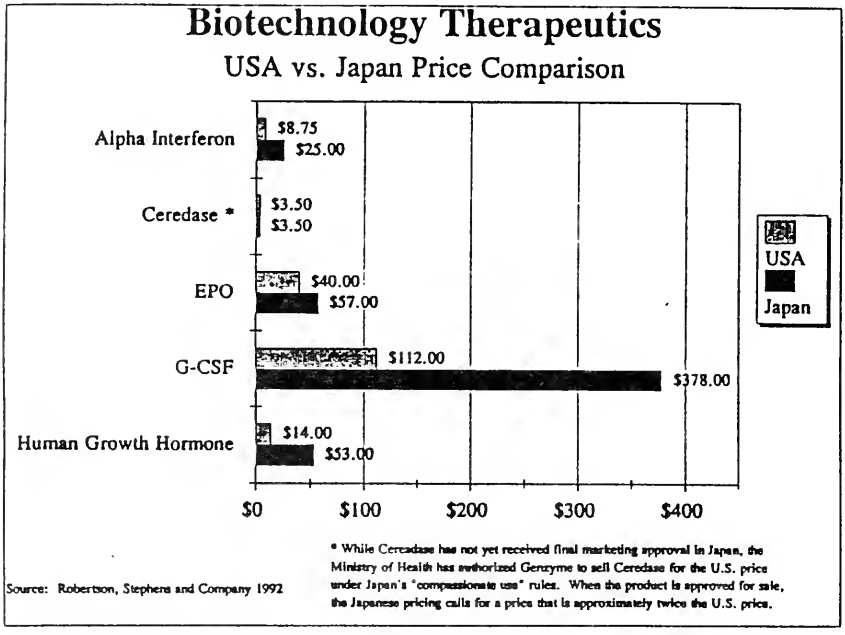
It is sometimes said that U.S. prices for drugs are higher than those for the same drugs abroad and that the U.S. is subsidizing the world's research on medicines. This is not true for biotech medicines,[6] which is a positive measure of our competitiveness in international markets.

[4] Feinstein Partners Incorporated, January 19, 1994.

[5] Ernst & Young, Biotech 94 Long Term Vale Short Term Hurdles, Eighth Annual Report on the Biotech Industry, 28–31 (1993).

[6] Those products whose sales and prices are controlled by the U.S. biotech company.

A 1992 study by the investment bank Robertson Stephens and Company compares international prices for the leading biotech drugs in the U.S. and Japan. It shows that the prices of these drugs tends to be much higher in Japan (which sets drug prices) than in the U.S., often three times as high. For example, Human Growth Hormone is priced at $14 in the U.S. and $53 in Japan.; G-CSF is priced at $112 in the U.S. and $375 in Japan; EPO is priced at $40 in the U.S. and $99 in Japan and Alpha Interferon is priced at $8.75 in the U.S. and $25 in Japan. Japan adopted this pricing policy because it prizes innovation and wants to develop a biotech industry that can compete with ours.



BIO is aware of only one case in which a biotechnology company charges a lower price for its drugs in a major developed country compared to the United States. That one case is a drug that sells for 9 percent less in Europe. However, that same drug sells for the same price in Cadada and for 65 percent more in Japan. In all other cases, the drugs are priced at the same price or a hiker price abroad.

If the Japanese provide an incentive for innovative biotech medicines, we had better think long and hard before we penalize that same innovation.

PRICING OF BREAKTHROUGH MEDICINES

Many are interested in how the biotechnology industry prices its breakthrough medicines. This is a critical competitiveness issue for our industry. The biotechnology industry does not have, and never has had, unlimited discretion to price its breakthrough products. We never will. The same is true of any other industry or company which creates a breakthrough on some technology, including computer chips, software or any other technology. The beauty of our free enterprise system is that there are always competitors who are ready to enter your market, make your product obsolete and take away your market share.

We believe that the health care market works when breakthrough drugs are developed. The market does not work when no breakthrough drugs are developed.

How breakthrough drugs are priced once they are developed is an issue only if the drugs are, in fact, developed.

In order to encourage biotechnology companies to develop breakthrough drugs, they must be able to charge a price for the drugs that will reward investors for the extraordinary risk they have taken in financing the research. If the companies cannot charge this price or if investors fear that they will not be permitted to do so, the research will not be funded and we will not see breakthrough drugs developed.

Some may wish that investors did not expect a return on their investment m biomedical research. Some may wish that investors would fund research even if they

did not receive a return on their investment. But, the government does not provide the funds to pay for the research. Government research sponsored by NIH is only one step in the research and development process. We must and do rely on the private sector to develop breakthrough drugs and it is one of the geniuses of the U.S. economy that our private sector is so innovative and practical. It is in the government's interest for the private sector to take the risk, invest its own money, navigate the FDA approval process and compensate its employees in speculative stock options.

Companies that do develop breakthrough drugs often feel market pressures as soon as they market the drug. The real period of exclusivity in the market is likely to be 2-4 years, not the 17 years of its patent. Once a drug is developed, it is remarkable how quickly other companies will develop other drugs that will compete with it. This was true for AZT and the price of AZT dropped precipitously when the competitors arrived on the market. The company certainly cannot charge a price that consumers or their insurers cannot or are unwilling to pay. HMO's are very tough bargainers with any supplier of medical services.

In addition to direct market pressure, companies also are sensitive to public controversy, criticism from Congress and the Administration, Congressional oversight hearings, and other types of protests. They all have an impact on pricing decisions. They are part of the "market" that determines drug and all other prices in our economy.

NEED FOR HEALTH CARE REFORM

BIO is a strong supporter of health care reform. We have not supported or opposed any of the pending health care reform bills. Rather, we have focused on the key issues that affect our sector of the health care industry.

We believe that health care reform is critical to the competitiveness of America. Our health care costs are high in comparison to those of our major competitors. We, as a nation, must find a way to contain costs while maintaining the unequalled quality of our health care system. The biotechnology industry can play a central role in lowering health care costs by developing effective treatments and cures for currently untreatable diseases which cost America billions of dollars each year.

BIO HEALTH CARE REFORM POSITION

Let me briefly outline BIO's position on the key issues that have been raised in the pending proposals.

Innovation: BIO believes that we do not have enough therapies and cures for diseases like cancer, AIDS, Alzheimer's, Cystic Fibrosis, Multiple Sclerosis, and a host of other deadly and costly diseases. One of the highest priority in developing a health care reform plan must be to encourage research on these therapies and cures.

Universal Coverage: BIO supports the need to provide universal coverage. Without universal coverage we will continue to see massive cost shifting from those who do not provide, to those who do provide, health insurance coverage. Universal coverage is in our humanitarian and economic interest. It gives an opportunity to expand preventative health care, which will lower our long-term costs. We applaud the leadership which the Chairman of this Subcommittee has shown in championing universal coverage.

Universal coverage and cost containment are critical issues; however, we need to focus on innovation as well. It does a patient little good if he or she can pay the hospital and doctor bills but there are fewer treatments or cures for their disease.

Employer Provided Insurance: BIO understands the critical role that employers should and must play in providing health insurance to their employees. Virtually all of our biotechnology companies provide health insurance to their employees.

Basic Research Funding: BIO supports an increase in the funding for the National Institutes of Health (NIH). The importance of NIH basic research is outlined in Lisa Conte's statement.

I would like to comment on how impressed I am with the sophisticated understanding of the Chairman about the commercialization of technology. His proposal, S. 1537, demonstrates an understanding of the risks that private enterprises must take to bring products to market, a balanced understanding of the respective roles of government basic research and private sector development, and the critical need for incentives for private commercial firms to invest their own funds in a project. We look forward to working with the Chairman of the Subcommittee on S. 1537 to reform the NIH CRADA process.

Prescription Drug Benefit: BIO supports inclusion of a drug benefit as a part of a standard benefit package, and the provision of a prescription drug benefit for Medicare beneficiaries. Without such a benefit we will continue to see some of our elder-

ly unable to afford the medicines that will improve their quality of life and continued cost shifting between medicines and other medical costs. BIO supports inclusion of a prescription drug benefit in any standard benefit package for non-Medicare individuals for the same reasons.

Market Based Competition and Cost Containment: BIO supports market based competition to contain health care costs. We are confident that biotech medicines will be found to be both effective and cost effective by payers, doctors and patients. We are ready to compete in the current health care marketplace and to compete in a marketplace where buyers groups are even more powerful. We expect it will be tough, but we have effective and often unique products to sell. We are not afraid of competition based on patient outcomes.

Non-Cost Values: BIO cautions that we should not focus only on financial issues. If we do we will neglect some fundamental values. If a patient is likely to die, the least costly and most cost-effective strategy is probably not to treat them at all and to let them die as quickly as possible. This is not health care; this is euthanasia. A health care system focusing only on financial issues, as important as they are, is not a health care system that any of us can support.

Technology Assessment and Private Sector Medicare Drug Benefit: Let me devote the remainder of my statement to two issues where BIO has actively developed its own proposals: enhancing technology assessment and a private sector delivery system for the Medicare drug benefit. These are both proposals that we have outlined to the Administration and others working on health care reform and look forward to integrating them into the final legislation.

COST EFFECTIVENESS OF BIOTECHNOLOGY MEDICINES

Biotechnology medicines should be a critical element of any cost containment strategy. This is consistent with the fundamental values of our economic system, which look to innovative technologies in order to lower costs and improve our quality of life.

The most cost effective health care we can provide is safe and effective drugs and vaccines. Some surgery can be vastly more expensive. Hospital stays can be more expensive.

If we eliminated all costs—not just profits, but all costs—for breakthrough drugs, we would have an impact on 3 percent of the 7 percent of the total health care budget that comes from breakthrough drugs. Three percent of 7 percent is 0.2 percent, a few billion dollars. If we eliminated only the profit of breakthrough drugs, the savings would be a fraction of that amount.

The effectiveness of biotech medicines is high. GM-CSF, a treatment of Hodgkin's disease, has a cost of $6,700. However, use of this treatment for a patient with Hodgkin's disease results in a net savings of $16,000 when compared with other treatments.[7] Interferon Alfa-2B, a treatment for hairy cell leukemia, has a cost of $3,364. However, if this treatment is used rather than other existing therapies, there is a net savings of $9,019.[8] Finally, Neutropenia, a biotechnology medicine which treats cancer patients that develop low white blood counts and fevers as a result of chemotherapy, costs $2,300 per cycle. However, since the medicine reduces hospitalization, its use can save $8,470.[9]

ENHANCING TECHNOLOGY ASSESSMENT

BIO supports enhancing, expanding, and refocusing the medical technology assessment activities of the U.S. government. We do not fear such assessments as long as they focus on the full range of medical interventions that are available to treat a disease or condition.

The principal government medical technology assessment agency is the Agency for Health Care Policy and Research ("AHCPR"). AHCPR (1) increases the availability of information and data concerning the value and cost of all medical treatments, including quality of life and cost effectiveness to providers, payers, and patients; (2) encourages use of the appropriate technology and discourages the excessive utilization of all technology; and (3) promotes the development of breakthroughs and other technological advances that benefit patients over their lifetimes and lower costs.

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[7] Gulati, S.C. and Bennett, C.L.: "Granulocyte-macrophage colony-stimulating factor (GMF-CSF) as adjunct therapy in relapsed Hodgkin's disease." Annals of Internal Medicine, Vol. 116, No. 3 (1992 February 1): 177-182.

[8] Ozer, H. et al., "Cost-Benefit Analysis of Interferon Alfa-Ab in Treatment of Hairy Cell Leukemia." Journal of the National Cancer Institute, Vol. 81, No. 8 (1989 April 19): 594-602.

[9] Glaspy, J. et al. "The Economic Impact of Recombinant Granulocyte Colony-Stimulating Factor." Health Systems—The challenge of Change. Proceedings of the 5th International Conference of Systems Science in Health Care. Editors: Chytil, M.K. et al. Omni Publishers. Prague.

It is an appropriate role of the federal government to develop and disseminate information and data on patient outcomes and the appropriate uses of technology in lowering costs and improving the quality of life. Private sector companies will not always agree with the judgments or analysis of an agency like AHCPR; they may find them ctuu1ly inaccurate or worse. But, we are realistic and know that the government will continue to develop and disseminate this information. The issue is how well it performs this function in a rational manner.

AHCPR is not the only agency or entity which analyzes these issues. University professors, health care professionals, private insurance companies, HMOs, and a host of others already develop and disseminate this information. BIO would not support a system where only a government agency could or would develop and disseminate this information. However, we are not troubled by the idea that the government is one of many which perform this function.

It is also a legitimate function of government to: strengthen the research base on the effectiveness and cost-effectiveness of medical technology; set priorities for such research; provide funding for research and technology assessments; facilitate the development of patient practice guidelines; assure the systematic evaluation of existing and new treatments and technologies; and widely disseminate its findings and recommendations to all health care providers, payers, and patients.

It is critical that the final decisions about whether and how to use a particular technology should be made by local providers and their patients, in consultation with local plans and scientific research. The information and data disseminated by the government and other sources will and should play a role in these decisions, but not as mandates. The government should not interfere with the doctor-patient relationship or limit the choices available to doctors and patients. The influence of the government will and should be based on the quality of its work.

A decision by local providers and their patients not to use a technology for a particular patient or a whole plan should be based on persuasive evidence that the excluded therapy does not present a clinically meaningful advantage over the available alternative therapies.

The government should not assume that it knows best which technology should be utilized. It doesn't know and it should not presume to think that it does.

Government technology assessments should be made by an agency in which providers, payers and patients can have confidence in its scientific assessments. Such confidence would not be justified if technology assessment is the responsibility of an agency that makes decisions regarding cost containment or benefit design. Decisions concerning research commissioned by the agency should be based on the peer review procedures in effect at agencies like NIH. Politicization of the assessments or research grants will undermine confidence and stall the adoption of the assessments in the private sector.

All technologies and procedures, including biotechnology medicines, should be subject to possible evaluation and re-evaluation at any time. We would not ask for an exemption for medicines created by the biotechnology industry. Priorities for assessments and research should be set where there is a wide range of treatment options at substantial differentials in cost.

It makes less sense to focus all of the technology assessment on a product at the moment it is being introduced. In most cases, assessments can be made with more information after the product has been utilized in the real world market. At its point of introduction, we will know more about its cost and much less about its effectiveness and cost effectiveness. This is the least appropriate and useful time to assess a technology.

The simple fact that a new technology has been introduced does not justify immediate review, let alone intensive review. If we do require that technology undergo such review at this critical point in the product development cycle, we will, in effect, set up a third requirement for its approval: safety, effectiveness and then something else. This will increase the cost of development, discourage research, and delay utilization of new technology.

We should not fear new technology. We should seek it. We should not set up a system which is biased against new technology. We should focus on its effectiveness in treating disease. That is the medical bottom line. It is a fundamentally more important consideration than the cost of the technology.

Technologies subject to FDA review (drugs, biologics, devices) should be presumed to be safe, effective, and not investigational for uses which have marketing approval or are accepted uses listed in the major compendia. We do not need duplication of this review. The FDA review is lengthy and expensive enough.

Procedural safeguards should be set by statute to discourage arbitrary actions by payers in decisions of providers and payers and to give consumers and other inter-

ested parties the right to challenge adverse decisions regarding utilization of technology.

AHCPR or other agencies which perform this function should be funded at a level appropriate to ensure that they can effectively carry out their objective. To ensure funding, alliances, the principal consumers of the agency's assessments and other re:arch, could be required to pay user fees to the agency.

Assessment strategy such as I have outlined can enhance the competitiveness of the U.S. biotechnology industry. A system that is biased against breakthrough biotechnology medicines would dramatically undermine our competitiveness.

CONCLUSION

There is no subcommittee in the Congress that better understands the value of technology than this subcommittee.

Many of the policy issues mentioned in Lisa Conte's statement—FDA user fees, the Biotechnology Patent Protection Act, technology transfer policies and tax policies—are vitally important to the biopharmaceutical industry. I have focused on the special issues which affect our sector of the biotechnology industry, emphasizing our views on health care reform.

The biotechnology industry knows that it will create medicines that are effective and cost effective. We are seeking to create breakthroughs in the treatment of cancer, AIDS, Alzheimer's, and a host of other deadly and costly diseases. That is our business, our inspiration, and our contribution to reducing the cost of health care in America, thus increasing our competitiveness.

We are reasonable and practical. That is essential to our survival as entrepreneurs. We do not fear assessments of our products. We may not always agree with them, but we are confident that our products will find a market with doctors and patients who care about the quality of health care. Such assessments should not, however, presume that we are the principal cost containment problem or priority.

America should rely on the biotechnology industry to improve the quality of our health care system and contain costs. We need a national bias in favor of breakthrough medicines.

Our industry is the paradigm of the high-tech, high-research, high-risk emerging industry that we all know is the hope for America. We cannot expect to compete based on how low our wages are; we have to compete with our brains.

BIO strongly support universal coverage. We want a reasonable opportunity to find cures and therapies for diseases like cancer. That is our goal and we want a fighting chance in the market place to achieve it.

We look forward to working with the Technology Subcommittee to fashion a health care plan that encourages innovation. This is your jurisdiction, your expertise, and your issue. We commend your leadership on this critical issue.

Senator ROCKEFELLER. Thank you.

What strikes me as odd in all of this is we spent—and you two were not here, but we spent all of last week in what I thought was somewhat of an infantile debate over something called—which people chose to call "industrial policy." And what today has been the story of, in some sense, is the story of Government and the biotechnology industry working together.

And I think last year it was about $4.3 billion that went from the U.S. Treasury into your industry in an aggregate sense. And it disturbs me that people—and, of course, we have done the same thing with agriculture, we have done the same thing with aerospace, we have done the same thing with, you know, a lot of other--semiconductors, all kinds of things, where the country has deemed something to be severely in the national interest, a critical technology so to speak, and certainly biotechnology is a critical—listed as a critical technology.

So, it is disturbing when you have so many policymakers, or in this case Senators, including, many from my own party who would probably be known generally as very enlightened. And I asked them why did you vote against this? And they say, "Well, the Government has no business getting involved in what industry is

doing, and if industry cannot make it on its own then it probably is not worth doing."

And everything I have heard today is just standing testimony to the opposite of that, that you have to get a start. Venture capital has not exactly been a stirring success in our country in the last 10 years or so—people have kind of become risk averse, like insurance companies—and Government can help and Government does help in these things.

But you indicated, Mr. Skaletsky, a little bit your concern also in the health care thing. That, if I read between the lines correctly, that there is some sense of nervousness about the Government getting into price controls, or am I misreading you?

Mr. SKALETSKY. No, you are not misreading me at all. I am concerned about it, and the concern I have is the impact it will have on innovation. Our companies are innovative companies, our goal is to develop new medical treatments, and we have no problem with people looking at us and judging us against other available therapies, and other available treatments for diseases. And I think the AHCPR option is a very interesting one, looking at the disease itself and what are the options to treat the disease, whether it is through drugs or through surgery, or do nothing, and have that data available for people to make judgments based on all of that information, as opposed to having just a drug price and decisions being made on that. And that is the concern I have with the proposals.

Senator ROCKEFELLER. But it is interesting to me. I happen to be the person who started AHCPR in legislation back in 1989 in so-called physician payment reform, and it has therefore had a relatively short history. And it is doing quite well and it is beginning to turn out, you know, practice guidelines in some very good areas, and it is gradually getting known.

Now, for AHCPR to put something out and for the medical community to accept it and implement it, those are two different steps. But I just worry, I worry about the problem of perception, because if that really is not our intent and the Government at some point does have a responsibility—I mean this is insulting to even make a comparison, but when we do not pay attention sometimes things go awry, and the savings and loan crisis was an example of that which cost the people one-half a trillion dollars and it is going to be a trillion dollars, $2 trillion, who knows, by the time it is finished. And that just eviscerates the national ability to educate our kids and clean up our environment and get your microbes working in the right places.

So, I worry about that, because that is not the intent, it is not the intent. We have something called a Physician Payment Review Commission which advises the Congress on the appropriateness of what it is that physicians under Medicare are being paid. We have something called PROPAC which is an advisory commission to Congress which looks at what is going on in hospitals and what their charges and what their costs are.

And I do not think that hospitals and doctors look upon these as hostile entities, and they are actually doing something probably a lot more visible than what this particular breakthrough commission would be doing. Because the physician payment reform makes

recommendations to the Congress. It has an activist role and it is, by law, required to make recommendations; this other breakthrough price commission does nothing of the sort.

So, this question of perception is very troubling because I remember when the stocks were going down and I was talking to a biotechnology person who was just absolutely furious at me. And he said, "You know, my stocks are just tumbling and they are in a freefall," and then low and behold, you know, several weeks, several months later, they came right back up, and that is the way things work in our society. People do not trust Government. Government makes a suggestion. We are in financial crisis. We are trying to reduce the deficit. We are pumping billions into your industry in an aggregate sense; you are not complaining about that.

And so I do not know. It disturbs me because I think that the degree of focus of the pharmaceutical industry and the biotechnology industry, when it decides that it does not like something, that it says so so loudly and so strongly, it creates the self-fulfilling prophecy. You know that, in a sense, you lower your own stocks because you make such an issue of something which, in fact, may not become an issue at all, or if it does become an issue, may, in fact, deserve to become an issue, because it will be 1 out of every 10,000 ideas, it will be outrageously priced.

I mean you have people in your industry, as we do in mine, who take advantage of situations, and part of the responsibility of Government is to make sure—is to protect public interest on these things. Do either of you care to respond to that?

Mr. PEREZ. I would like to say something with regard to small business, but first you keep talking about perception and at times perception turns into reality. And we can make it so. We can make whatever is perceived turn into reality if we all keep thinking in that direction. And it could be good or it could be bad.

But small business, where I come from, is scared to death of this health reform, I think because we do not know enough about it.

Senator ROCKEFELLER. You mean not necessarily the breakthrough drug price commission, but just the whole thing in general?

Mr. PEREZ. I am talking about the whole thing. I cannot talk from the pharmaceutical end. I can only talk from the small businessman's perception. And small business is a major part of the economy in the United States, as we all know.

Senator ROCKEFELLER. It is most of it.

Mr. PEREZ. Most of it, that is correct.

Our company, we calculate, with just 140 employees—it will be approximately $250,000 extra a year is what we think the health care plan will impact on us, having to pay for 80 percent of the health care program.

Just as a sidebar, in Germany, I think theirs is the highest that we have run across, and theirs is a 50–50-type of split over in Germany. I believe that is the highest.

But most of the small business people I talk to do not understand it, and are just afraid of it from one standpoint—they know something has to be done. We do not know what has to be done—or how to solve the problem. But whatever it is is going to cost the businesses. And there is no place to pass it on. Businesses—it is like

environmental cleanups, the major companies that we work for have a line item in their budget for environmental cleanups. Well, that goes into their product and is passed along to their customers.

Well, most of the companies of small businessmen, whether they are running a restaurant or running a biotechnology company, have no place to pass it on. In our company, for example, foreign competition—competition out of Taiwan, Japan, Germany, and France is keeping our margins stabilized. We cannot raise our margins at all. So, any line item that hits us, in terms of health care, in terms of anything else, has to be taken right out of our margins.

So, I believe that from our standpoint, from a small business person's standpoint, we fear the unknown. The unknown is what is it going to cost us? We do know that something has to be done. Something has to be done.

Senator ROCKEFELLER. Do you provide health insurance for your employees now?

Mr. PEREZ. Absolutely, yes, sir.

Senator ROCKEFELLER. Then what you ought to be terrified of Mr. Perez not doing anything. Your premiums, I am going to bet you, went up 25 percent last year.

Mr. PEREZ. Absolutely, I totally agree with you. Yes, sir, about 22.5 percent.

And we are. We are afraid. Something has to be done. This is what I said, we do not know what, but something has to be done. And the fear is, what is it going to cost us? And where is it going to start impacting businesses?

You have heard of the old saying, 49 and holding, I know business people that have 49 employees and refuse to add any more employees. The reason is because you go into new types of Government controls when you have 50-plus employees.

So, as a small business person, you are going to try to find a way around it if it has very much of an adverse impact on you. So, we are like you. We do not know what to do, but we know that something has to be done. And everybody is trying to protect their own interests.

Senator ROCKEFELLER. Yes. OK.

Mr. SKALETSKY. Senator, if I could come back to the issue of the breakthrough drug price controls. One of the wonderful things about our economy is the way it can react to situations that happen in the market.

Using the example of Gaucher's Disease and this drug Ceredase, since it has been introduced—and 10 other companies refused to develop it—the NIH went to 10 companies and asked them to develop it and they said "No, the market is not large enough"—3 companies are now in the process of developing alternative treatments to Gaucher's Disease. And when they are available, market forces will take care of it—competition. And we have that in our industry. And I think that is a healthy thing.

The other piece of this is the perception that you are talking about from investors. I think it is important to remember the layers of risk that investors look at in our industry—finding a molecule, developing it, getting it out into the market—if we add to that other layers of risk, it is going to force these people to think

again about why should I invest in this industry, I can invest in Boston Chicken.

It is the same people, public investors who invest in our companies that invest in some of the retail companies. So, we are competing for their money.

Senator ROCKEFELLER. Biotechnology, I have it here somewhere, what was the increase in profitability as a national aggregate figure in the last couple of years? Do you have any idea?

Mr. SKALETSKY. I am told we went down 3.6.

Senator ROCKEFELLER. You went down?

Mr. SKALETSKY. Yes, year to year.

Senator ROCKEFELLER. With your business of 17 employees?

Mr. SKALETSKY. Oh, I am sorry—our industry.

Senator ROCKEFELLER. Biotechnology in general?

Mr. SKALETSKY. Yes.

Senator ROCKEFELLER. Is the stock market?

Mr. SKALETSKY. That is the operating loss of the industry.

Senator ROCKEFELLER. Sales went up, and that is in my figures here.

Mr. SKALETSKY. Yes.

Senator ROCKEFELLER. Sales went up 17 percent. So, how does the other work out?

Mr. SKALETSKY. Sales went up 17 percent, obviously, because more products were approved by the FDA. The other issue there is that many of our companies, those who have sales, take that profit and put it right back into R&D to develop new products. And so that is why, when we talk about our industry, there is only three or four companies in our entire industry, out of the 1,200, that are profitable. Many of us have not gotten to the point where we have sales so we can even imagine having profits. And even some of those who do have sales are still in a loss mode because they are pouring those profits, or that revenue, back into R&D.

Senator ROCKEFELLER. Is there anything else that the Government is doing or appears to be contemplating that makes you nervous, or is it this one particular thing in health care?

Mr. SKALETSKY. My own opinion is, generally, I think the Government is very supportive of our industry. And we look forward to working with the Government more and more. Sure there is little issues—this CRADA issue that you talked about before is something that I am sure can be worked out.

The patents, the patentability of our technology. I mean, we are confident that that will be worked out. And, again, we are not looking to be treated differently or unfairly in the eyes of some. We just really want an opportunity to develop our innovative products and get them out to be used for people who need them.

Senator ROCKEFELLER. Mr. Perez.

Mr. PEREZ. In the environmental industry, superfund is up for reauthorization. And we have recently found out that there is a weakening in some of the types of methods to deal with superfund sites, going from permanent types of problem solving to more temporary types. And it is a reduction in permanence.

For instance, instead of treating sites, we would look to contain sites. And we are working with the EPA, talking to them about how to somehow take care of the problem on a permanent basis as

opposed to going back and taking care of it on a nonpermanent basis, such as containment.

So, this is one of the things that I believe—by the way, taking care of a superfund site, which your State, along with every other State almost, has several superfund sites, taking care of it on a nonpermanent basis or on a containment basis is much cheaper. But what you are doing is, once again, passing along the old maid. At some point in time, those vaults, those slurries, whatever type of mechanism you use, will need to be remedied on a permanent basis.

And our position is to do it right the first time and not have to go back in with some other type of technology possibly and have to do it all over again.

So, this is one of the things we are working on.

Senator ROCKEFELLER. You both have been very, very hopeful. One thing I think that I should reflect on, in terms of the pharmaceutical industry—if the pharmaceutical industry is suspicious of the Government, the pharmaceutical industry has to understand that this Government has been really burned by the pharmaceutical industry.

And it goes back to a particular piece of legislation called catastrophic health care, where the Pharmaceutical Association of America, through some of the most brutal, expensive lobbying tactics that I have ever seen or heard of in my life, crushed that bill in their own interest. And you gentlemen have to recognize that. That there is a residue—not in me—because in the Senate I led the fight and we refused to repeal catastrophic—we had 73 votes that stood up against the pharmaceutical industry and we were successful based upon the merits—but they made themselves at that time a reputation which was so bad that they are still living it down.

And that is a factor, I think, in this sort of current uneasiness as between the two parties. I think, in fact, it is such a factor that the reason that Bill Gradison, who now is heading up the Health Insurance Association of America, which is putting out all of these ridiculous ads casting doubt on health care reform of any sort, really, I believe, quit the Congress. Because he was so disillusioned. Because he was part of creating an excellent bill. He was the Republican counterpart to creating an excellent bill, and it was thrown back in his face, fundamentally, by the PMA.

So, there is a very, very deep remembrance of that. So, it is not just the U.S. Government which has to evidently make a better case to the pharmaceutical industry about this, but it is the pharmaceutical industry which has to make a case to the U.S. Government as to why we should believe that we can trust their behavior.

Mr. SKALETSKY. Senator, I appreciate that. And I am sure you understand that——

Senator ROCKEFELLER. That is some truth in lending.

Mr. SKALETSKY. I am sure that you understand that at the time that that debate was going on, our industry virtually almost did not exist. And even today, we only have 23 products that are currently on the market. There are several thousand that are in the development stage.

One of the things that we like to think about ourselves as an industry—and you can talk to people at the FDA—they enjoy working with the biotechnology industry. It is a dialog back and forth.

Senator ROCKEFELLER. And I make a difference here, biotechnology and pharmaceutical.

Mr. SKALETSKY. And I appreciate that. And I hope you continue and we continue to get your support in that difference.

Senator ROCKEFELLER. Yes.

Mr. SKALETSKY. Thank you.

Senator ROCKEFELLER. This has been helpful.

I think we have had a very, very good conversation. I have learned a lot. And I think the exchange has been reasonable.

So, I thank you for coming from where you have come and for contributing to this debate.

Thank you all very much.

[Whereupon, at 4:55 p.m., the hearing was adjourned.]

APPENDIX

QUESTIONS ASKED BY SENATOR BURNS AND ANSWERS THERETO BY MR. SKALETSKY

Question. Tell me, if government price controls are implemented under any sort of health care reform plan, and capital shrinks, how will your company be specifically effected? Job layoffs? R&D slowed? Or will you be unable to bring your products to market?

Answer. If government price controls are implemented under a health care reform plan, the results to GelTex would be quite negative. We would not be able to develop our products as quickly as we now plan, as financing the development of those products would be much more difficult We would not be able to hire the necessary people into the company on a timely basis. Also, we would have to make very difficult decisions as to which products we will develop as we would not be able to develop more than two or three products with the limited resources available.

Question. I'll ask you the same thing I asked Ms. Conte. What can we do here in Congress to assure that biotech companies are able to continue researching and developing new products?

Answer. I believe that understanding the power and importance of biotechnology to the future of the United States is critical for Congress to appreciate. It is the responsibility of our industry to educate Congress and the general public as to what we are doing and its importance. We need Congress to be available to help us when the need arises.to secure the long term safekeeping of our technology in the United States. This can be in the form of patent reform, capital market issues, health care reform, etc. Additional information should be generated showing health care innovation reduces overall health care costs to society.

Question. In the past year, there have been a number of consolidations in the biotech industry and Japan is increasingly becoming a source of capital. What does this do to a start-up biotech company and is this a viable option?

Answer. The Japanese pharmaceutical industry continues to be very aggressive in the pursuit of American biotechnology companies that have interesting technology and/or products. The Japanese have a very long term view of drug development and are willing to commit large sums of monies to develop important products. The ability of biotechnology companies to negotiate licensing agreements with Japanese companies has become very important in this uncertain financial climate.

Question. We have heard what price controls will do to small biotech companies, but tell me in real numbers what this will mean for jobs and more importantly to the future of health care?

Answer. Price controls will have a devastating impact on the ability of our industry to develop innovative products. It has been shown that the best way to reduce health care costs is through innovation; the biotechnology industry can become a significant contributor to developing products to treat currently untreatable diseases. If we are faced with the issue of price controls, we will not be able to raise the capital necessary to continue development of these important products. The biotechnology industry currently employs approximately 100,000 people in the United States. Most of these people are involved in research and development as there are only a handful of products currently being marketed by the industry. As we continue to be successful in the development and approval of important new therapies, many companies will have to expand their employment levels to include manufacturing, sales, and marketing people. The total numbers will be several times the current levels.

QUESTIONS ASKED BY SENATOR BURNS AND ANSWERS THERETO BY MR. PEREZ

Question. We are doing a great deal of mine waste remediation research in Montana. Are you familiar with our projects?

Answer. Senator Burns, I am not familiar with the research projects in Montana, but I have directed my company in privately funded research to:

- Increase the leaching of mineral ores especially gold and silver from tailings pile for recovery.
- Immobilize certain heavy metals such as Lead and Chromium from water through a biomass concentration effect using a facultative anaerobic bacteria.
- Treat mine leachate wastewater containing Cyanides through fixed film reactors inoculated with P. Chryosporum.

As you can appreciate a small business like ours cannot adequately pursue microbial technologies as described above without private or public funding. when we are funded, the "strings" attached limit our publication and dissemination of technology. One feature we can provide any research group is our manufacturing capacity. We can grow bacteria, fungi, and yeast to concentrated cultures in dry and liquid form.

I would appreciate having your staff place me in contact with one or two of your leading Montana researchers in this field of study.

Question. Would you please explain how using microbes or bacteria can be used to clean up environmental pollution?

Answer. Bacteria and other microorganisms are everywhere in our world, but concentrate in places where there is an organic substrate, or food to enable their growth.

The bulk of environmental pollution In the U.S. Involves potential substrates for bacteria which are contained in a liquid (wastewater), gaseous (air), or solid (soil, rock, organic polymer) matrix. Almost every organic carbon molecule has been identified in scientific literature as being degradable by some microorganism.

Scientist and Engineer design reactors to optimize the growth of microorganisms, especially those which transform environmental pollutants to relative benign compounds such as carbon dioxide (CO_2) and water (H_2O). This optimization involves reactor configuration and design, provision of oxygen or other electron acceptors, and addition of nutrients such as nitrogen and phosphorus that microorganisms need to synthesize new cells.

Examples of how microorganisms are used in this application are:

- An activated sludge system in a refinery, treating oily wastewater.
- A biofilter or porous media reactor, which receives air contaminated with hydrogen sulfide and removes it prior to atmospheric release.
- A land farm, such as the Bozeman Superfund Site in Montana, where residual chemicals from wood treating are applied to soil containing bacteria and fungi, that mineralize them to CO_2 and H_2O.

Our company, ERI/Interbio allows actual control of the microbiology in the reactor. We produce concentrated microbial cultures (more than 3 billion organisms per gram) that can be added to these reactors in cases where indigenous microorganisms are inhibited by site conditions or toxicity of the chemical. ERI/Interbio has applied these bacteria to more than 500 waste treatment systems in every U.S. state, including Montana. These cultures are now used by consumers in septic tank treatment, grease trap control, carpet cleaning and a number of other applications where potentially toxic chemicals were previously used.

The potential of adding our acclimated microbes has been recorded by many including, Dr. Martin Alexander of Cornell University (formerly a member of the U.S. EPA) Scientific Advisory Committee, who described their ability to degrade Pentachlorophenol, Parathion, Chlorpropham, crude oils, PCB's, 2,4, 5T, and several other industrial chemicals and pesticides.

Question. Why is this environmental remediation using biotechnology Important to our nation?

Answer. Every business spends money to control pollution, directly and indirectly. After recycling and recovery have taken place there will also be some waste to discharge to the environment.

In the U.S. we have choices of how to handle these wastes: Containment or Landfilling; Thermal Oxidation or Incineration; and Bioremediation.

As a society we should reject Containment or Landfilling as a solution, except for those wastes which are so difficult to treat by the other two methods that we must maintain them for future technologies. Landfilling other wastes is similar to storing garbage in your garage. One day you will have to clean up again at a much more expensive cost. Today landfilling hazardous waste may cost $200-300/ton. Landfilling is not a cost effective technology.

Thermal Oxidation or Incineration is often technically feasible for low volume, high BTU wastes. It destroys the waste which is preferable to containment. Therefore, [illegible] of hazardous waste, which makes it [illegible] the public perception of incineration is so

bad,no one would consider one in his home town, no matter how safe he/she knew the technology to be.

Finally, Bioremediation, which is suitable for high volume, low BTU wastes is a low impact technology. We have participated in more than 50 public hearings to clean up a site and not received a disapproval one time. The cost for hazardous waste is less than $100/ton, which makes it attractive to the small businessman.

Biotechnology for environmental remediation has a definite place in the private sector. At the same time I note our currently proposed reauthorization of Superfund would favor strategy of containment rather than permanent strategies (as is currently part of the law) such as thermal treatment and bioremediation. Containment While providing some economic relief for those faced with large clean up cost will only pass the problem down to future generations. Permanent remedies such as Thermal Oxidation or Bioremediation will eliminate this waste as well as develop technologies which we can export to other countries.

In summary bioremediation technology is an affordable alternative for environmental clean up. It is much more popular on the private side than Superfund sites (which represent the worst waste problems in the nation) and is a technology sought after by -all the countries of the world to deal with their own environmental and infrastructure problems.

QUESTIONS ASKED BY SENATOR BURNS AND ANSWERS THERETO BY MR. JACOBSEN

Question. Would you please explain to the Subcommittee the work in biotech research you are doing at Montana State University.

Answer. Biotechnology research is being done in several colleges at Montana State University. These include the College of Agriculture, College of Lefters and Science, College of Engineering and the College of Education, Health and Human Development. Much of the research is by faculty and staff supported in -part by the Montana Agricultural Experiment Station. In addition, this research is funded by the State of Montana, NSF-EPSCoR, federal and private grants.

In the College of Agriculture, we currently have projects involving both plants and animals. In the plant biotechnology area, our work is focused on 1) genome mapping in barley, wheat and alfalfa, 2) plant variety improvement using genes identified in the genome research. This work involves cold hardiness, resistance to plant diseases and insects, herbicide resistance, and the development of varieties with unique nutritional, processing, or other characteristics. For example, one product of the genome mapping project is the identification of genes that will allow barley to have feed characteristics more similar to corn. Another is the development of safflowers with unique oil content (high oleic, high linoleic) which make them more valuable for specific end uses. We have also developed safflower lines with resistance to the broad spectrum environmentally friendly herbicide, glyphosate. This will allow for better weed control in safflower production.

The genome mapping projects will pay major dividends in breeding barley, wheat or alfalfa lines that are higher yielding, resistant to pests or environmental stresses such as drought or severe winters, produce unique biochemicals or even pharmaceuticals, or have unique processing or nutritional requirements.

Another major biotech research thrust is that of biocontrol. Presently we are investigating unique natural products and organisms for biocontrol of plant pests including insects, weeds and plant diseases. Examples are natural compounds that disrupt the life cycle of fungi that cause smut diseases such as TCK smut. microorganisms that control insects or weeds, and biorational compounds from plants that repel or suppress insect pests. Work is also underway with plant growth promoting rhizobacteria and rhizosphere inhabiting fungi that can be used as seed treatments to control root rots or improve nutrient or water uptake. In this past month we and Bozeman Biotech received an SBIR grant to commercialize a bacterial seed treatment for control of seed rot and seedling diseases in sweet corn and other vegetable crops. Control with this biological is equal to synthetic chemical fungicides.

MSU is also using biotech in a wide range of animal projects. Research currently in progress involves detection and therapy for a number of animal disease problems and basic research in understanding animal parasite and pathogen interactions with their hosts. In cooperation with USDA scientists at Fort Keogh, there are projects involving beef cattle genome and reproductive endocrinology.

Attached is a list of Montana Agricultural Experiment Station projects underway in biotech research. As you can see, we have 37 scientists with more than $1 million in state funding involved. [This information may be found in the committee files.]

Question. What about biotech research at the Northern Plains Soil and Water Research Station—Sidney on leafy spurge.

Answer. Dr. Neal Spenser, USDA/ARS entomologist is conducting important research in the use of introduced insects for control of leafy spurge in eastern Montana and western North Dakota. This research is critical since it is in a very different environment than scientists located in Bozeman. In addition, there is work on biological control of grasshoppers. Again this is a unique and important environment. While biological control holds much promise it must be custom designed (researched) to fit different environments.

Finally, as you know, the Montana Agricultural Experiment Station at Sidney shares physical facilities with the USDA/ARS unit. The research we have on producing safflower varieties with unique fatty acid profiles (high oleic acid, high linolenic acid, etc.) would be impossible without this facility.

Question. Why is the biotech research you do important nationwide?

Answer. While research here at MSU focuses on crops and problems of the high plains and the Northwestern U.S., this research will and has contributed to new products such as vaccines and diagnostic tests for animal diseases that occur throughout the nation. We are developing new crop varieties that will provide new export income as well as renewable resources for "green chemistry" based industrial processes. In addition, the basic research yields new techniques and ideas that are used by researchers elsewhere in the U.S.

MSU is a leader in crop improvement for wheat, barley, alfalfa, and safflower, all crops grown elsewhere in the U.S. Our successes impact producers far beyond Montana. We are also a leader in the biological control of noxious weeds, insect pests, and plant diseases. Once again the methods and the products of this research have impacts across the entire U. S. Finally, our graduate students are hired by universities, businesses, and government agencies across the country.

The biotech research done at MSU and elsewhere is critical to bringing new value-added jobs to both rural and urban areas and in producing a renewable resource based industry for the future—one not dependent on nonrenewable resources. Biotechnology will reduce our dependence on synthetic chemical pesticides while allowing our farmers to produce both high yields and quality. This is critical as the world becomes more dependent on fewer farmers.

Biotechnology is critical to the economic future of the U.S. and the world. It will produce new products for human medicine, and animal or crop production. It will provide the basis for new food products that contribute to our health and will provide the basis for new crops and markets for our agricultural producers.

QUESTIONS ASKED BY SENATOR BURNS AND ANSWERS THERETO BY MS. CONTE

Question. I understand the biotech market lost 40 percent of its value when health care reform became a reality. What did this drop do to existing companies, to start-ups, and how is the market now?

Answer. The drop in value for the biotechnology capital markets has had a profound impact on the biotechnology industry. First of all, numerous biotech companies have had to layoff workers. For example, over the last year, Scios Nova has eliminated 44 positions, Somatagen has eliminated 24 positions, Cryomedical Sciences cut back 15 positions and Cytogen has cut back 58 positions. In addition, biotechnology companies have had to curtail research into various areas. A survey taken by the Biotechnology Industry Organization late last year showed that almost half of its member companies conducting AIDS research had to slow down their efforts because of a lack of available capital. Another survey in February of this year, focusing on cancer research, showed a similar pattern. Finally, preliminary results from a survey of companies conducting research into aging-related diseases show that almost one third have had to delay or curtail research. All of these cut- backs were attributed to the threat of price controls as part of the Administration's health care reform proposal.

The outlook for the future of the industry is becoming more discouraging. In a survey conducted by the Gordon Public Policy Center at Brandeis University, 75 percent of the biotech companies responding said that they had less than 2 years capital left at their current burn rates. Thirty-four percent had less than 1 year of capital left. In addition, the capital market for biotech companies has continued to be depressed in 1994. According to BioCentury, the biotech industry raised $223.8 million in initial public offerings (IPOs) during the first quarter of 1993, compared with $196.5 million in 1994, a 12 percent decline. For secondary offerings, during the first quarter of 1993 the industry raised $391.5 million, compared with $327.3 million during the first quarter of 1994, a 16 percent decline. Overall, the industry

has raised 10 percent less during the first quarter of 1994 than it did during the first quarter of 1993. When you take into account that the American Stock Exchange Biotechnology Index lost approximately 40 percent in 1993, you can see that the market for biotech companies is currently in a state of decline.

Question. Almost 50 percent of the new funds going into the marketplace go into seed and second-stage type companies. If venture capitalists continue to fund new ventures and not support existing ventures, what do you see happening to R&D?

The goal of venture capital is not to fund a company though the entire process of researching and developing a drug, bringing a drug through the regulatory process, and then bringing that product to market. This process can not be sustained by venture capital alone. It has been estimated by the Office of Technology Assessment (OTA) that it costs approximately $359 million to develop a drug. Biotechnology companies need to rely on the public capital markets as they get closer to market because this is when the approval process becomes more expensive. The role of venture capital is to help a company begin the process of researching a compound that may become a therapeutic or cure. When the company demonstrates efficacy enough to merit an initial public offering (IPO) for the company, venture capitalists usually sell their stake in the company. Therefore the fact that venture capitalists are still funding seed and second-stage companies is not unusual. Therefore, the effect will be to create more competition as more companies become ready to file for IPOs, however it will not stunt research and development in the biotech industry.

Question. What can we do here in Congress to assure that biotech companies are able to continue researching and developing new products?

Answer. The biotechnology industry must confront numerous obstacles on the way to bringing products to the market. Only 5 out of 4,000 compounds screened in preclinical testing make it to human testing and only 1 of those 5 is approved for the market. In addition, the FDA process is an expensive and lengthy one, the ability to obtain financing is constantly being threatened, and there is an incredible amount of competition in the industry because of the number of companies. If you add to these obstacles price controls for products that do make it to the market, you will be seriously damaging the long-term prospects for the industry. Congress can help the biotechnology industry by repudiating the one obstacle it has the power to change, price controls. There is no question that price controls are a threat to the future of our industry. We ask for Congress not to allow the Advisory Council on Breakthrough Drugs and the blacklisting authority given to the Secretary of Health and Human Services to be enacted as part of any health care reform bill.

Question. I know capital is tough to come by and it is not solely the fault of health care reform. Products can take 10-12 years from development to approval. Few are willing to invest in a company that has potential earnings in the year 2004. Is this a cautious government making sure products are safe, or is this the quagmire of bureaucracy? How do you propose we deal with this problem?

The safety and efficacy of new drugs that are admitted to the market must be thoroughly tested. However, the FDA process has become increasingly difficult for companies to traverse as regulations get more complicated and lengthy. Is it important that the FDA process is closely examined in order to determine that it is best for both the consumer and the company. One of the reasons that the process is lengthy is that the FDA is asked to examine more products than it is capable of handling. This problem is only going to become worse. Ernst & Young estimates that there are 270 therapeutics in human clinical development and over 2,000 in early development stages. In order to help the FDA increase its capacity, and to accelerate the approval process, the biotechnology industry has agreed to User Fees. These were designed to be earmarked only for the FDA drug approval process. FDA has had problems hiring new physicians because of the Vice President's' Reinventing Government Initiative. It is important that the User Fee program is evaluated regularly in order to ascertain whether it is indeed helping. Congress must also work to make sure that the User Fee program is successful and that the review of drugs at the FDA becomes a quicker process.

Question. How do we unfreeze the frozen capital markets?

Answer. There are several obstacles that biotechnology companies must navigate before they become successful. The risk that is involved for both the investor and the company is enormous. For the industry to be successful and to have the ability to raise capital, it must produce innovative products that meet currently unmet needs. Product failures during the last year have had an impact on the markets. The risk involved has had and will continue to have an impact on the markets. However, the one factor that Congress and the Administration have the power to change is price controls. The threat of price controls has had a large impact on the capital markets for the biotechnology industry. It is extremely important that Con-

gress does not enact price controls, whether direct or indirect, as part of any health care reform bill.

QUESTIONS ASKED BY SENATOR BURNS AND ANSWERS THERETO BY MR. GREENWOOD

Question. What is the Clinton Administration's position on the direction that biotechnology use should take in this country?

Answer. As I mentioned in my statement, biotechnology offers an extraordinary range of applications that extends across several industries. The earliest applications arose in the health care and pharmaceutical industries, primarily because the methods that comprise biotechnology—DNA cutting and splicing, cloning, production of monoclonal antibodies, etc., are the result of basic biomedical research. Thus the people responsible for the development of techniques that make it possible to manipulate the building blocks of life, naturally were the first to employ them, first for research purposes, and then to make novel drugs and therapeutics. One prime example is the advent of gene therapy, which is being used to treat certain forms of cancer, such as advanced melanoma, or some of the more than 5,000 inherited disorders such as cystic fibrosis or Gaucher's disease.

The next set of researchers to adopt the new tools of biotechnology were in the agriculture industry, using them to create hardier pest- and disease-resistant crops and foods with better nutritional profiles, or fibers with better yield and durability and easier harvesting characteristics.

Today we are seeing applications in energy production through the development of renewable alternatives to petroleum products. Manufacturing has turned to biotechnology for less expensive and cleaner ways to make fine chemicals or biodegradable alternatives to plastics that don't require petroleum derivatives. Biotechnology offers innovative means to restore polluted environmental sites, to degrade toxic materials and to replace chemical pesticides with environmentally benign biocontrol agents.

How should we use these tools? I think the answer is carefully, but with an appreciation for the enormous promise of biotechnology to create high-value added jobs, to enhance our economic growth and to improve the quality of our lives and our environment.

Question. Do you understand the need to continue federal support for biotechnology research funding as a way to reduce this country's reliance on pesticides for food and fiber production?

Answer. I do indeed, and I particularly appreciate your phrasing of this question when you sac "reduce" rather than eliminate reliance on pesticides. The reason that I say this is that there are groups or individuals who believe that the only way to reduce reliance on pesticides is to go "cold turkey." That any interim measures that involve the use of safer, more environmentally benign pesticides, for example, is not worthwhile. I believe that there is ample evidence to support the development and approval of pesticides that do not persist in the environment, that have a narrower spectrum of toxicity or that are better targeted to specific pests, thus allowing more harmful chemicals to go out of use.

Federal support for this research is an important element of the development and eventual commercialization of these desirable products.

Question. It is my understanding that the President's budget proposes to cut nearly $800,000 for funding for biotech research at the Northern Plains Soil and Water Research Station in Sidney, Montana while funding $2.6 million for the European Biological Control Laboratory in Montpelier, France. Does this make sense to you?

Answer. The USDA Northern Plains Soil and Water Research Center at Sidney, Montana, does not conduct biotechnology research in the context of fundamental cellular and molecular biology. The program emphasis at Sidney is research on dryland crop production and conservation systems and biological control of rangeland weeds. It is true that the President's FY 1995 budget proposes to close this Center along with 18 other Agricultural Research Service (ARS) laboratories nationwide. These reductions are part of the Administration's efforts to achieve government program and management efficiencies while allowing reinvestment of available research resources for addressing national problems in the broad public interest such as food safety and pesticide use reduction. Research similar to that now conducted at Sidney, Montana, addressing Northern Great Plains agricultural problems will be continued at other nearby ARS laboratory locations, including Bozeman, Montana; Mandan, North Dakota; Cheyenne Wyoming; and Akron, Colorado.

The ARS European Biological Control LAboratory in Montpelier, France, also serves the Northern Great Plains in an important way in that it is the primary

source of natural biological agents from Europe that are imported to Montana and other states for control of leafy spurge and other agricultural pests. The $2.6 million increase requested in the President's FY 1995 budget for the ARS Montpelier, France, laboratory is a one-year appropriation to construct a new facility to accommodate the consolidation of two separate ARS biological control programs formerly located at Paris, France, and Rome, Italy.

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